Barb O'Bryen

Considered 12/17/02

Access DB# 79291 mc

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: My-Chau Tram Examiner #: 78733 Date: 11/4/02
Art Unit: 1639 Phone Number 305-6999 Serial Number: 09/944,083
Mail Box and Bldg/Room Location: CM1, 8A16 Results Format Preferred (circle): PAPER DISK E-MAIL
4D 3B01

If more than one search is submitted, please prioritize searches in order of need. ME1

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods for Generating Ligand Arrays via Deposition of Ligand onto olefin displaying substrates and arrays produced

Inventors (please provide full names): Steven M. Lefkowitz; Nam yong Kim; Nelson R. Holcomb; John S. Hargreaves; Geraldine F. Dellinger; Douglas J. DeEllinger

Earliest Priority Filing Date: 8/31/01

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Mrs. O'Bryen

Please perform inventors search and the flowing key words:

1) DNA chip or microarray
2) different oligonucleotides or polynucleotides
3) functional group: a) benzaldehyde
   b) carboxylate ester
   c) amine
   d) imidazolyl carbamate

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

Attached is Abstract as aid

Thank you

****

STAFF USE ONLY Type of Search Vendors and cost where applicable

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=> fil capl; d que l37; d que l39; d que l41
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inventor search

FILE COVERS 1907 - 8 Nov 2002 VOL 137 ISS 20
FILE LAST UPDATED: 7 Nov 2002 (20021107/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L37            0 SEA FILE=CAPLUS ABB=ON  DELLINGER G?/AU

L33           96 SEA FILE=CAPLUS ABB=ON  LEFKOWITZ S?/AU
L34         2572 SEA FILE=CAPLUS ABB=ON  KIM N?/AU
L35           10 SEA FILE=CAPLUS ABB=ON  HOLCOMB N?/AU
L36          204 SEA FILE=CAPLUS ABB=ON  HARGREAVES J?/AU
L38           30 SEA FILE=CAPLUS ABB=ON  DELLINGER D?/AU
L39            2 SEA FILE=CAPLUS ABB=ON  (L33 AND ((L34 OR L35 OR L36) OR L38))
                 OR (L34 AND (L35 OR L36 OR L38)) OR (L35 AND (L36 OR L38)) OR
                 (L36 AND L38)

L1          1148 SEA FILE=CAPLUS ABB=ON  DNA(2A)(CHIP? OR MICROCHIP?)
L2          9384 SEA FILE=CAPLUS ABB=ON  MICROARRAY?
L3          1621 SEA FILE=CAPLUS ABB=ON  BIOCHIP?
L4           287 SEA FILE=CAPLUS ABB=ON  LAB-ON-A-CHIP/CT
L33           96 SEA FILE=CAPLUS ABB=ON  LEFKOWITZ S?/AU
L34         2572 SEA FILE=CAPLUS ABB=ON  KIM N?/AU
L35           10 SEA FILE=CAPLUS ABB=ON  HOLCOMB N?/AU
L36          204 SEA FILE=CAPLUS ABB=ON  HARGREAVES J?/AU
L38           30 SEA FILE=CAPLUS ABB=ON  DELLINGER D?/AU
L41            7 SEA FILE=CAPLUS ABB=ON  ((L33 OR L34 OR L35 OR L36) OR L38)
                 AND (L1 OR L2 OR L3 OR L4)

=> s l39 or l41

L155           8 L39 OR L41

=> fil wpids; d que l48;d que l50
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FILE 'WPIDS' ENTERED AT 10:12:25 ON 08 NOV 2002
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FILE LAST UPDATED:          5 NOV 2002      <20021105/UP>
MOST RECENT DERWENT UPDATE:     200271        <200271/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI run number 70 for WPI was inadvertently processed with
    a wrong ED/UP date resulting in empty answer sets.
    Therefore SDI 70 will be rerun tonight.  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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L42           20 SEA FILE=WPIDS ABB=ON  LEFKOWITZ S?/AU
L43         1508 SEA FILE=WPIDS ABB=ON  KIM N?/AU
L44            2 SEA FILE=WPIDS ABB=ON  HOLCOMB N?/AU
L45           37 SEA FILE=WPIDS ABB=ON  HARGREAVES J?/AU
L46            1 SEA FILE=WPIDS ABB=ON  DELLINGER G?/AU
L47           21 SEA FILE=WPIDS ABB=ON  DELLINGER D?/AU
L48            3 SEA FILE=WPIDS ABB=ON  (L42 AND ((L43 OR L44 OR L45 OR L46 OR
                 L47))) OR (L43 AND ((L44 OR L45 OR L46 OR L47))) OR (L44 AND
                 ((L45 OR L46 OR L47))) OR (L45 AND (L46 OR L47)) OR (L46 AND
                 L47)



L42           20 SEA FILE=WPIDS ABB=ON  LEFKOWITZ S?/AU
L43         1508 SEA FILE=WPIDS ABB=ON  KIM N?/AU
L44            2 SEA FILE=WPIDS ABB=ON  HOLCOMB N?/AU
L45           37 SEA FILE=WPIDS ABB=ON  HARGREAVES J?/AU
L46            1 SEA FILE=WPIDS ABB=ON  DELLINGER G?/AU
L47           21 SEA FILE=WPIDS ABB=ON  DELLINGER D?/AU
L49         2500 SEA FILE=WPIDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?
                 OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L50            2 SEA FILE=WPIDS ABB=ON  (L42 OR L43 OR L44 OR L45 OR L46 OR
                 L47) AND L49


=> s l48 or l50

L156           5 L48 OR L50

=> fil biosis; d que l72; d que l77; d que l79

FILE 'BIOSIS' ENTERED AT 10:12:28 ON 08 NOV 2002
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.
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RECORDS LAST ADDED: 7 November 2002 (20021107/ED)

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L72          0 SEA FILE=BIOSIS ABB=ON  HOLCOMB N?/AU


L71       1389 SEA FILE=BIOSIS ABB=ON  KIM N?/AU
L73        181 SEA FILE=BIOSIS ABB=ON  HARGREAVES J?/AU
L74          4 SEA FILE=BIOSIS ABB=ON  DELLINGER G?/AU
L75         13 SEA FILE=BIOSIS ABB=ON  DELLINGER D?/AU
L76        149 SEA FILE=BIOSIS ABB=ON  LEFKOWITZ S?/AU
L77          1 SEA FILE=BIOSIS ABB=ON  (L71 AND (L73 OR L74 OR L75 OR L76))
               OR (L73 AND (L74 OR L75 OR L76)) OR (L74 AND (L75 OR L76)) OR
               (L75 AND L76)


L71       1389 SEA FILE=BIOSIS ABB=ON  KIM N?/AU
L73        181 SEA FILE=BIOSIS ABB=ON  HARGREAVES J?/AU
L74          4 SEA FILE=BIOSIS ABB=ON  DELLINGER G?/AU
L75         13 SEA FILE=BIOSIS ABB=ON  DELLINGER D?/AU
L76        149 SEA FILE=BIOSIS ABB=ON  LEFKOWITZ S?/AU
L78       5511 SEA FILE=BIOSIS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
               BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L79          2 SEA FILE=BIOSIS ABB=ON  (L71 OR (L73 OR L74 OR L75 OR L76))
               AND L78


=> s l77 or l79

L157         3 L77 OR L79

=> fil jic; d que l91;d que l92; d que l93; d que l94; d que l96

FILE 'JICST-EPLUS' ENTERED AT 10:12:34 ON 08 NOV 2002
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FILE COVERS 1985 TO 5 NOV 2002 (20021105/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.


L91          0 SEA FILE=JICST-EPLUS ABB=ON  DELLINGER G?/AU


L92          0 SEA FILE=JICST-EPLUS ABB=ON  DELLINGER D?/AU


L93          0 SEA FILE=JICST-EPLUS ABB=ON  LEFKOWITZ S?/AU


L94          0 SEA FILE=JICST-EPLUS ABB=ON  HOLCOMB N?/AU


L89        202 SEA FILE=JICST-EPLUS ABB=ON  KIM N?/AU
L90          1 SEA FILE=JICST-EPLUS ABB=ON  HARGREAVES J?/AU
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L95         443 SEA FILE=JICST-EPLUS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L96           0 SEA FILE=JICST-EPLUS ABB=ON  (L89 OR L90) AND L95


=> fil biotechno; d que l115;d que l117; d que l121; d que l122

FILE 'BIOTECHNO' ENTERED AT 10:12:35 ON 08 NOV 2002
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FILE LAST UPDATED: 7 NOV 2002       <20021107/UP>
FILE COVERS 1980 TO DATE.

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     /CT AND BASIC INDEX  <<<


L115          0 SEA FILE=BIOTECHNO ABB=ON  HOLCOMB N?/AU



L117          0 SEA FILE=BIOTECHNO ABB=ON  DELLINGER G?/AU



L114        212 SEA FILE=BIOTECHNO ABB=ON  KIM N?/AU
L116         26 SEA FILE=BIOTECHNO ABB=ON  HARGREAVES J?/AU
L118          3 SEA FILE=BIOTECHNO ABB=ON  DELLINGER D?/AU
L119          5 SEA FILE=BIOTECHNO ABB=ON  LEFKOWITZ S?/AU
L121          0 SEA FILE=BIOTECHNO ABB=ON  (L114 AND (L116 OR L118 OR L119))
                OR (L116 AND (L118 OR L119)) OR (L118 AND L119)



L114        212 SEA FILE=BIOTECHNO ABB=ON  KIM N?/AU
L116         26 SEA FILE=BIOTECHNO ABB=ON  HARGREAVES J?/AU
L118          3 SEA FILE=BIOTECHNO ABB=ON  DELLINGER D?/AU
L119          5 SEA FILE=BIOTECHNO ABB=ON  LEFKOWITZ S?/AU
L120       3621 SEA FILE=BIOTECHNO ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L122          2 SEA FILE=BIOTECHNO ABB=ON  (L114 OR L116 OR L118 OR L119) AND
                L120


=> fil biotechds; d que l135; d que l137; d que l140; d que l142

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L135          0 SEA FILE=BIOTECHDS ABB=ON  HOLCOMB N?/AU



L137          0 SEA FILE=BIOTECHDS ABB=ON  DELLINGER G?/AU
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L134          40 SEA FILE=BIOTECHDS ABB=ON  KIM N?/AU
L136           3 SEA FILE=BIOTECHDS ABB=ON  HARGREAVES J?/AU
L138           6 SEA FILE=BIOTECHDS ABB=ON  DELLINGER D?/AU
L139           2 SEA FILE=BIOTECHDS ABB=ON  LEFKOWITZ S?/AU
L140           0 SEA FILE=BIOTECHDS ABB=ON  (L134 AND (L136 OR L138 OR L139))
                 OR (L136 AND (L138 OR L139)) OR (L138 AND L139)



L134          40 SEA FILE=BIOTECHDS ABB=ON  KIM N?/AU
L136           3 SEA FILE=BIOTECHDS ABB=ON  HARGREAVES J?/AU
L138           6 SEA FILE=BIOTECHDS ABB=ON  DELLINGER D?/AU
L139           2 SEA FILE=BIOTECHDS ABB=ON  LEFKOWITZ S?/AU
L141        2598 SEA FILE=BIOTECHDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                 BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L142           5 SEA FILE=BIOTECHDS ABB=ON  (L134 OR L136 OR L138 OR L139) AND
                 L141


=> dup rem l155,l157,l122,l142,l156
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PROCESSING COMPLETED FOR L155
PROCESSING COMPLETED FOR L157
PROCESSING COMPLETED FOR L122
PROCESSING COMPLETED FOR L142
PROCESSING COMPLETED FOR L156
L158          11 DUP REM L155 L157 L122 L142 L156 (12 DUPLICATES REMOVED)
                 ANSWERS '1-8' FROM FILE CAPLUS
                 ANSWERS '9-10' FROM FILE BIOTECHDS
                 ANSWER '11' FROM FILE WPIDS

=> d ibib ab 1-11

L158 ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2002 ACS        DUPLICATE 1
ACCESSION NUMBER:         2002:158329  CAPLUS
DOCUMENT NUMBER:          136:196540
TITLE:                    Synthesis and use of biological conjugate sensors
INVENTOR(S):              Dellinger, Douglas J.; Myerson, Joel;
                          Fulcrand, Geraldine; Ilsley, Diane D.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 20 pp., Division of U.S. Ser.
                          No. 397,526.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002025539	A1	20020228	US 2001-981580	20011017

PRIORITY APPLN. INFO.: US 1999-397526 A3 19990916
OTHER SOURCE(S): MARPAT 136:196540

AB The invention concerns methods for conjugating one moiety to another moiety. In the method, the moieties are reacted with one another in a protic solvent. Reaction between the moieties and the protic solvent during the conjugating is negligible or reversible. A stable bond is formed between the moieties to produce a product that is not subject to .beta.-elimination at elevated pH. Usually, one of the moieties comprises an unsatn. between two carbon atoms. One of the carbon atoms is or becomes an electrophile during the conjugating. The other of the moieties comprises a functionality reactive with the electrophile carbon atom to form a product that comprises the unsatn. Compds. comprising both of the moieties as well as precursor mols. are also disclosed. Methods are also disclosed for detg. an analyte in a sample employing compds. as described above.

L158 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:183821 CAPLUS
DOCUMENT NUMBER: 136:211865
TITLE: Method for hybridization of arrays on siliceous surfaces
INVENTOR(S): Shannon, Karen W.; **Lefkowitz, Steven M.**
PATENT ASSIGNEE(S): Agilent Technologies Inc. (A Delaware Corporation), USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1186671	A2	20020313	EP 2001-121185	20010904

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 2000-655482 A 20000905

AB A method (100, 200) of hybridizing arrays of nucleic acids an surface-derivatized siliceous substrates with other nucleic acid materials provides an envelope of conditions to produce sensitive, selective detection of nucleic acid targets, while preserving the intactness of the derivatized surface of the array. The envelope of hybridization conditions includes a hybridization soln. having a pH between pH 5.5 and 6.7 and a high hybridization or incubation temp. between 55.degree.C and 70.degree.C. In one embodiment (100), the hybridization soln. is maintained (102) at the pH between pH 5.5 and 6.7 and the array is incubated (104) with a nucleic acid material in the pH-maintained hybridization soln. at the hybridization temp. of between 55.degree.C and 70.degree.C. The pH of the hybridization soln. is maintained (102) with a buffer having a useful buffering capacity between pH 5.5 and 6.7. In another embodiment (200), a nucleic acid material is combined (202) with the hybridization soln. at the pH between pH 5.5 to 6.7 contg. a buffer and a monovalent cation and the combined soln. is incubated (204) with the array at the hybridization temp. of between 55.degree.C and 70.degree.C so as to hybridize the nucleic acid material. Typical hybridization times can range from less than 2 h to more than 48 h. The present method is particularly useful for hybridization assays an silylated-siliceous substrates where the incubation time is much greater than about 6 h at the high hybridization temp. The envelope of hybridization conditions provide

optimized assay performance while maintaining the integrity of the derivatized surface of the siliceous substrate. A kit comprises a **microarray** having a siliceous substrate with a derivatized surface and an oligonucleotide populated an the surface for hybridizing a another oligonucleotide material. The kit further includes instructions for using the **microarray** in accordance with the method (100, 200) of the present invention.

L158 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2002:639382 CAPLUS
TITLE: Gene expression profiling of osteoclast differentiation by combined suppression subtractive hybridization (SSH) and cDNA **microarray** analysis
AUTHOR(S): Rho, Jaerang; Altmann, Curtis R.; Socci, Nicholas D.; Merkov, Lubomir; **Kim, Nacksung**; So, Hongseob; Lee, Okbok; Takami, Masamichi; Brivanlou, Ali H.; Choi, Yongwon
CORPORATE SOURCE: Abramson Family Cancer Research Institute, Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA, USA
SOURCE: DNA and Cell Biology (2002), 21(8), 541-549
CODEN: DCEBE8; ISSN: 1044-5498
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bone homeostasis is maintained by the balanced action of bone-forming osteoblasts and bone-resorbing osteoclasts. Multinucleated, mature osteoclasts develop from hematopoietic stem cells via the monocyte-macrophage lineage, which also give rise to macrophages and dendritic cells. Despite their distinct physiol. roles in bone and the immune system, these cell types share many mol. and biochem. features. To provide insights into how osteoclasts differentiate and function to control bone metab., we employed a systematic approach to profile patterns of osteoclast-specific gene expression by combining suppression subtractive hybridization (SSH) and cDNA **microarray** anal. Here we examd. how gene expression profiles of mature osteoclast differ from macrophage or dendritic cells, how gene expression profiles change during osteoclast differentiation, and how Mitf, a transcription factor crit. for osteoclast maturation, affects the gene expression profile. This approach revealed a set of genes coordinately regulated for osteoclast function, some of which have previously been implicated in several bone diseases in humans.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:843827 CAPLUS
DOCUMENT NUMBER: 136:1554
TITLE: Immobilization of oligonucleotides or other ligands on glass surfaces via amine group-terminated or hydroxy group-terminated alkylene imines
INVENTOR(S): Fulcrand, Geraldine; **Dellinger, Douglas J.**; **Lefkowitz, Steven M.**
PATENT ASSIGNEE(S): Agilent Technologies, Inc., USA
SOURCE: U.S., 31 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 6319674	B1	20011120	US 1999-397527	19990916

OTHER SOURCE(S): MARPAT 136:1554

AB Methods are disclosed for immobilizing a substance to a surface. A surface is employed that comprises a linking group consisting of a first portion comprising a hydrocarbon chain, optionally substituted, and a second portion comprising an alkylene oxide or an alkylene imine wherein the alkylene is optionally substituted. One end of the first portion is attached to the surface and one end of the second portion is attached to the other end of the first portion chain by means of an amine or an oxy functionality. The second portion terminates in an amine or a hydroxy functionality. The surface is reacted with the substance to be immobilized under conditions for attachment of the substance to the surface by means of the linking group. Compns. of matter and reaction systems are also disclosed.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER: 2001:499771 CAPLUS
DOCUMENT NUMBER: 135:94015
TITLE: Functionalization of substrate surfaces with silane mixtures
INVENTOR(S): **Lefkowitz, Steven M.**; Fulcrand, Geraldine; **Dellinger, Douglas J.**; Hotz, Charles Z.
PATENT ASSIGNEE(S): Agilent Technologies Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6258454	B1	20010710	US 1998-145015	19980901
US 2001051221	A1	20011213	US 2001-897340	20010702

PRIORITY APPLN. INFO.: US 1998-145015 A3 19980901

AB Low surface energy functionalized surfaces on solid supports are provided by treating a solid support having hydrophilic moieties on its surface with a derivatizing compn. contg. a mixt. of silanes. A first silane provides the desired redn. in surface energy, while the second silane enables functionalization with mol. moieties of interest, such as small mols., initial monomers to be used in the solid phase synthesis of oligomers, or intact oligomers. Mol. moieties of interest may be attached through cleavable sites. Derivatizing compns. for carrying out the surface functionalization process are provided as well. Thus, a compn. comprising 97.5% n-decyltrichlorosilane as a first silane and 2.5% undecenyltrichlorosilane (I) as a second silane was used to functionalize a glass substrate, followed by boration and oxidn. to convert the terminal olefinic moiety of the surface-bound I to a hydroxy group.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

ACCESSION NUMBER: 2001:260533 CAPLUS
DOCUMENT NUMBER: 135:327876
TITLE: Expression profiling using **microarrays** fabricated by an ink-jet oligonucleotide synthesizer
AUTHOR(S): Hughes, Timothy R.; Mao, Mao; Jones, Allan R.; Burchard, Julja; Marton, Matthew J.; Shannon, Karen W.; **Lefkowitz, Steven M.**; Ziman, Michael; Schelter, Janell M.; Meyer, Michael R.; Kobayashi,

Sumire; Davis, Colleen; Dai, Hongyue; He, Yudong D.; Stephaniants, Sergey B.; Cavet, Guy; Walker, Wynn L.; West, Anne; Coffey, Ernest; Shoemaker, Daniel D.; Stoughton, Roland; Blanchard, Alan P.; Friend, Stephen H.; Linsley, Peter S.
CORPORATE SOURCE: Rosetta Inpharmatics, Inc., Kirkland, WA, 98034, USA
SOURCE: Nature Biotechnology (2001), 19(4), 342-347
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe a flexible system for gene expression profiling using arrays of tens of thousands of oligonucleotides synthesized in situ by an ink-jet printing method employing std. phosphoramidite chem. We have characterized the dependence of hybridization specificity and sensitivity on parameters including oligonucleotide length, hybridization stringency, sequence identity, sample abundance, and sample prepn. method. We find that 60-mer oligonucleotides reliably detect transcript ratios at one copy per cell in complex biol. samples, and that ink-jet arrays are compatible with several different sample amplification and labeling techniques. Furthermore, results using only a single carefully selected oligonucleotide per gene correlate closely with those obtained using complementary DNA (cDNA) arrays. Most of the genes for which measurements differ are members of gene families that can only be distinguished by oligonucleotides. Because different oligonucleotide sequences can be specified for each array, we anticipate that ink-jet oligonucleotide array technol. will be useful in a wide variety of DNA **microarray** applications.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:367211 CAPLUS
DOCUMENT NUMBER: 136:366140
TITLE: Method of shielding biosynthesis reactions from the ambient environment on an array using a nonmiscible fluid
INVENTOR(S): Perbost, Michel G. M.; **Lefkowitz, Steven M.**
PATENT ASSIGNEE(S): Agilent Technologies, Inc., USA
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387636	B1	20020514	US 1999-426823	19991022
US 2002086327	A1	20020704	US 2002-43590	20020109

PRIORITY APPLN. INFO.: US 1999-426823 A3 19991022
AB A method of fabricating an array of biopolymers provides a shield for biochem. reactions and biochem. reactants and is particularly useful for those reactions and reactants that are susceptible to reaction with a component of the ambient environment during the fabrication of the array. The method is applicable to the conventional fabrication and synthesis methods used to fabricate a biopolymer array, such as in situ synthesis of biopolymers on an array and the attachment of pre-synthesized biopolymers on to an array. The method comprises applying a non-miscible fluid (NMF) to the array surface where the biopolymers are being synthesized or attached. The NMF is inert and insol. with the biochem. reactants and other ancillary materials in soln. used in conventional synthesis or attachment of biopolymers. The NMF provides a shield between the ambient

atm. and the biopolymer synthesis materials or the deprotected pre-synthesized biopolymer at the surface of the array during the synthesis or attachment processes. The NMF may be applied as droplets over each feature location on the surface or may be applied by flooding the surface of the array to fully cover the features. Biomonomer or biopolymer solns. are deposited into or through the NMF to the feature locations on the surface of the array where the synthesis or attachment reactions are to take place using conventional deposition equipment to eject the solns. into the NMF. The NMF provides a shield for activated biomonomers that are susceptible to reaction with a component in the ambient environment, such as moisture in the air. Moreover, the NMF provides a shield for pre-synthesized biopolymers that are susceptible to evapn. when deprotected for attachment to the array surface. The method provides a means by which the potential reactivity of the activated biomonomer or deprotected biopolymer with an ambient atm. component can be kept low. As a result, biopolymer arrays can be more accurately fabricated. The NMF is selected from a group consisting of heptane, octane, nonane, decane, undecane, dodecane, tridecane, tetradecane, pentadecane, hexadecane, heptadecane, cycloheptane, cyclooctane, cyclononane, and cyclodecane.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:464296 CAPLUS
DOCUMENT NUMBER: 135:43095
TITLE: Methods and devices for carrying out chemical reactions
INVENTOR(S): Gordon, Gary B.; **Dellinger, Douglas J.**
PATENT ASSIGNEE(S): Agilent Technologies, Inc., USA
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6251595	B1	20010626	US 1998-100152	19980618
US 2001036641	A1	20011101	US 2001-842482	20010425

PRIORITY APPLN. INFO.: US 1998-100152 A3 19980618

AB Methods and devices are disclosed for carrying out multiple chem. reactions. A plurality of electrodes supported by a semiconductor substrate is brought into proximity with a reaction medium, which comprises reagents for carrying out the chem. reactions. An item of numerical data is sent to storage means in each of a plurality of cells within the semiconductor substrate by means of a data bus. The item of numerical data is representative of an elec. signal. An address is sent to address decoders in communication with the storage means. As a result, the item of numerical data is stored in the storage means. Elec. signals are selectively applied to each of the electrodes by means of a plurality of digital analog converters, each elec. coupled to a resp. electrode. Each of the digital analog converters is assocd. with a resp. cell. In this way, a chem. reaction takes place proximal to and in response to the field at the electrodes to which the elec. signals are selectively applied. A particular feature of the present invention is that the medium may be non-aq. The reagents are esp. ones for carrying out synthesis of oligonucleotides.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L158 ANSWER 9 OF 11 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-14804 BIOTECHDS
TITLE: Stably conjugating 2 groups that will not suffer beta-elimination at high pH, for labeling and surface attaching biomolecules, comprises reaction in a protic solvent where any reaction between solvent and group is negligible or reversible;
with application in DNA immobilization and DNA labeling
AUTHOR: **DELLINGER D J**; MYERSON J; FULCRAND G; ILSLEY D D
PATENT ASSIGNEE: DELLINGER D J; MYERSON J; FULCRAND G; ILSLEY D D
PATENT INFO: US 2002025539 28 Feb 2002
APPLICATION INFO: US 1999-981580 16 Sep 1999
PRIORITY INFO: US 2001-981580 17 Oct 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-303289 [34]

AB DERWENT ABSTRACT: NOVELTY - Conjugating (M1) one group to another, comprising reacting them with one another in a protic solvent where the reaction between the groups and the solvent is negligible or reversible, and a stable bond is formed between the groups to produce a product that is not subject to beta-elimination at elevated pH, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) conjugating (M2) one group to another, comprising: (a) combining them in a reaction medium where one of the groups comprises an unsaturated bond between two carbon atoms and one of the carbon atoms is or becomes an electrophile during the conjugating and the other group is able to react with the electrophile carbon atom to form a product comprising the unsaturation; and (b) subjecting the medium to conditions allowing formation of the product; (2) a compound of the formula (I); (3) a compound of the formula (II); (4) a compound of the formula (III); (5) determining (M3) an analyte in a sample, comprising: (a) combining the sample with (I) in a medium, where (I) forms a complex related to the presence of the analyte in the sample; and (b) detecting (I) in the complex, which indicates the presence of the analyte; (6) conjugating (M4) one group to another comprising: (a) combining reagents of formula (IV) and (V); and (b) treating the above combination to allow a conjugated product to form; and (7) conjugating (M5) one group to another, where the group is a ligand, receptor or surface, comprising: (a) combining reagents of formula (VI) and (VII) in an aqueous reaction medium; and (b) treating the above combination to allow a conjugated product to form having the formula (VII). M1 = a first group; L2', L3', L4'' = a bond or a linking group; R3, R4, R5, = a second group, or when not a second group are a hydrogen, alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroalkyl, heteroalkenyl, heteroaryl, and heteroaralkyl, or when R3 and R4 or R3 and R5 are not a second moiety, R3 and R4, or R3 and R5 may be taken together to form a 5 - 7 membered ring; and Y = a C=C , a carbon heteroatom double bond or a C-N triple bond, and when Y is C=C or a carbon heteroatom double bond, Y may be taken together with R3 or R4 to form a 5 -7 membered ring when R3 or R4 are not a second group. M1' = first group; M2' = second group; and L4' = bond or linking group. M2' = a group; L4' = a bond or linking group; and X' = fluoro, bromo, chloro or iodo. M1-L1-Z (IV) M1 = a first group; L1 = a bond or a linking group; and Z = a nucleophile. R, R1 or R2 = a second group, but when not a second group are independently an aliphatic or aromatic moiety, or when R and R1 or R and R2 are not a second group, R and R1 or R and R2 may be taken together to form a 5 -7 membered ring L2, L3 and L4 = a bond or a linking group; X = a leaving group, or X and R1 may be taken together to form a bond; and Y = a substituent that renders the carbon bearing the L2R group an electrophile, and also may be taken with R or R1 to form a 5 - 7 membered ring when R or R1 are not a second moiety. M1'-L1'-Z' (VI) M1 = a first group; L1 = a bond or a linking group; and Z = an amine group. M2' = a second group; X' = fluoro, bromo, chloro or iodo; and L1' and L4' = a bond or linking group. USE - The method is useful for the covalent attachment of one group to another, which is useful in the

labelling of a protein, peptide, polysaccharide, hormone, nucleic acid, label, antigen, or hapten. It is also useful in attaching these substances to a surface (all claimed). This is useful for tests such as chromatography, flow cytometry, mass spectrometry, and in the preparation e.g. of **micro-arrays** for use in enzyme-linked immunosorbent assays. ADVANTAGE - The invention allows two groups to be stably conjugated together in a solvent, and side reactions between the groups and the solvent are negligible or reversible, compared to previous methods of surface attachment and bio-conjugation which were susceptible to solvolysis problems. EXAMPLE - 5'- or 3'-amine-terminated oligonucleotides were dissolved in 0.05 M sodium carbonate buffer (pH 9.0) containing 0.005% Triton x-100 at a concentration of 10microM. The oligonucleotides were spotted onto the surface via pipette, pin or inkjet. The spots were allowed to dry and then were inspected visually for the appearance of salt crystals. The surfaces were placed into a humid chamber and the spots were allowed to re-hydrate. The attachment reaction was allowed to proceed for 12 hours; then, the surfaces were removed from the chamber and the spots were allowed to dry once again. The excess DNA was removed from the surface and the unreacted functional groups were passivated by treatment with a glycine solution. The surfaces were placed in a Teflon slide holder, and the holder was placed in a beaker containing 0.5 M sodium glycinate, pH 11.0 (+0 0.005% Triton X-100) for 20 minutes under stirring. The surfaces were washed with copious amounts of deionized water over a period of 5 min. This wash step was repeated 2 times. The surfaces were dried by centrifugation. (20 pages)

L158 ANSWER 10 OF 11 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-05978 BIOTECHDS
TITLE: Kit for mycobacterial species identification and drug resistance detection, has oligonucleotide chip with species identification probe, a mycobacterial drug-resistance detection probe, and its contrast group probe;
DNA chip, fluorescently-labeled **DNA** probe, DNA primer and polymerase chain reaction for Mycobacterium sp. rpoB gene detection
AUTHOR: KIM H; **KIM N**; YOON S; KIM J; PARK M
PATENT ASSIGNEE: BIOMEDLAB CO LTD
PATENT INFO: WO 2001092573 6 Dec 2001
APPLICATION INFO: WO 2000-KR904 30 May 2000
PRIORITY INFO: KR 2000-29369 30 May 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-075472 [10]
AB DERWENT ABSTRACT: NOVELTY - A diagnostic kit (I) for mycobacterial species identification and drug resistance detection comprising an oligonucleotide chip (II) including a species identification probe (P1), a mycobacterial drug-resistance detection probe (P2), a contrast group probe (P3) corresponding to each drug resistance detection probe, and a marker (III) for detecting a hybridization of (II) and a specimen, is new. DETAILED DESCRIPTION - A diagnostic kit (I) for mycobacterial species identification and drug resistance detection comprising an oligonucleotide chip (II) including a species identification probe (P1) comprised of species-specific DNA sequences of mycobacterial rpoB gene (157 bp), a mycobacterial drug-resistance detection probe (P2) comprised of one or more modified codons of mycobacterial rpoB gene (157 bp), and a contrast group probe (P3) comprised of wild-type sequences corresponding to each P2, and a marker (III) for detecting a hybridization of (II) and a specimen. INDEPENDENT CLAIMS are also included for the following: (1) manufacturing (M1) (I) comprising modifying P1, P2 and P3 to contain an amine group; inducing an aldehyde group on glass; and fabricating an oligonucleotide chip by affixing the modified probes on the glass with a Schiff base reaction, respectively; and (2) a pair of primers (IV)

comprising base sequences of 5'-biotin-tgcacgtcgcggacctcc-3' and 5'-tcgccgcgatcaaggagt-3' which specifically amplifies rpoB gene fragments (157 bp) of species belonging to Mycobacterium. BIOTECHNOLOGY - Preferred Kit: P2 comprises one or more modified codons of 507-533 codons of rpoB gene, preferably a rifampin-resistance detection probe which comprised modified 511, 513, 516, 518, 522, 526, and 531 codons, or further comprises modified 509, 533 and 524 codons, or rifabutin susceptibility detection probe which comprised modified 516 and 526 codons. (II) is preferably formed by a Schiff base reaction of each probe comprised of portion of rpoB genes modified to contain an amine group and an aldehyde group induced on glass. (I) further comprises components for amplifying DNAs of the specimen, which is preferably primers which include biotin-TR8 and TR9 primers; or biotin-DGR8 (tgsacgtcrcgnacytc) and DGR9 (tbgcsgcbatyaaggart), which amplify rpoB gene fragments (157 bp) specifically. (II) further comprises a Mycobacterium complex probe which can detect whether a specimen is Mycobacterium such as tuberculosis, where the probe is preferably: (1) tcttcggcaccagccag (2) tcttcggaaccagccag (3) tcttcggaacgtcgcag; and (4) tcttcggaacctcgcag. (III) is preferably a fluorescent material including the biotin-binding protein, more preferably streptavidin-R-phycoerythrin; or is Cynine 5-dUTP (added in the polymerase chain reaction). P1, P2 and P3 preferably comprises T10 included at 5' as a spacer. Preferred Method: (M1) further comprises reducing a fixed imine bond formed in the (M1) by NaBH4. USE - (IV) is useful for mycobacterial species identification and drug resistance detection. The method comprises amplifying rpoB gene fragments of specimen by Polymerase Chain Reaction (PCR) using (IV) and discriminating species by fluorescent intensity corresponding to a particular species by using (I), where PCR is performed at annealing temperature of 64-65degreesC for a period of 38-42 hours, with a primer concentration of 50-100 pmol, and PCR further comprises step of adding Cynine 5-dUTP as a marker; and the specimen is preferably uncultured sputum, blood or cerebrospinal fluid of a patient. (M1) is useful for manufacturing (I) (claimed). ADVANTAGE - Using (I), the Mycobacterium species identification and drug resistance detection can be discriminated rapidly and accurately in large quantity. (IV) enables efficient Polymerase Chain Reaction (PCR) amplification of rpoB gene fragments of numerous species directly from uncultured specimen. Drug resistance detection as well as Mycobacterium species detection can be performed simultaneously utilizing (I). EXAMPLE - The Mycobacterium complex probes which included Mc1 (5'Amine-T10-tcttcggcaccagccag 3'), Mc2 (5'Amine-T10-tcttcggaaccagccag 3') and Mc5 (5'Amine-T10-tcttcggaacgtcgcag 3'); Mycobacterium species identification probes having Mycobacterial species-specific DNA sequences of Mycobacterium rpoB gene which included: (1) ggtctgtcacgtgagcgtg; (2) ggtctgtcccgtgagcgtg; (3) ggtctgtcgcgtgagcgtg; (4) ggtctgtcccgggagcgtg; (5) ggtctgtcccgcgagcgtg; (6) ggtctgtcgagcgagcgtg; (7) ggtctgacccgtgaccgtg; and (8) ggtctgagccgggagcgtg. Mycobacterium drug-resistance detection probes including one or more modified codons of the rpoB gene which included: (1) cagccagccgagccaat; (2) gctgagcccattcatgg; (3) attcatggtccagaaca; (4) attcatgtaccagaaca; (5) tggaccagcacaacccg; (6) caacccgatgtcggggt; (7) caacccgctgttggggt; (8) ggttgacctacaagcgc; (9) ggttgaccgacaagcgc; (10) ggttgacccgcaagcgc; (11) ccgactgttggcgctgg; (12) attcatggagcagaaca; (13) ggttgaccaacaagcgc; (14) ggttgaccgccaagcgc; (15) ggttgacctgcaagcgc; (16) ggttgacccagaagcgc; and (17) ggttgaccggcaagcgc. Contrast group probes including wild type sequences corresponding to each drug resistance detection probes, probe Mex (5'Amine-T10-tcttcggaacctcgcag 3') detecting Corynebacterium diphtheria, which is not mycobacteria but belongs to similar but different genus as a contrast group in order to compare hybridization signal to each other, and additional species identification probes, MTAB (5'Amine-T10-gcagctgagccaattcat 3') and MF (5'Amine-a10-cgacgtcgcagctgtcg 3') were devised to specifically detect M. tuberculosis, M. africanum, M. bovis, M. bovis BCG, M. intracelluare, M. kansasii, M. fortuitum, and M. flavescens, were modified and were made to

contain an amine group at 5' terminal. Then, an aldehyde group was introduced on silylated slide glass and the modified probe was affixed on the glass by Schiff base reaction to obtain an oligonucleotide **chip**. Mycobacterial genomic **DNA** extracted from ten clinical isolates were amplified by PCR utilizing primers 5'-biotin-tgcacgtcgcggacctcc-3' and 5'-tcgccgcgatcaaggagt-3'. The resulting PCR product (157 bp) was treated with DNase I, and then hybridized with the oligonucleotide chip under optimal conditions. Then, the chip was stained with streptavidin-R-phycoerythrin for subsequent fluorescence scanning at 570 nm. The resulting image was analyzed for drug-resistance by comparing the fluorescent intensities of the wild-type probes with those of the mutation probes relatively. Results showed that the target DNA of mutant showed stronger signal on the corresponding mutant probe than its wild type probe.(74 pages)

L158 ANSWER 11 OF 11 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-328102 [36] WPIDS
CROSS REFERENCE: 2001-615254 [71]
DOC. NO. NON-CPI: N2002-257372
DOC. NO. CPI: C2002-094732
TITLE: Derivatizing composition useful for preparing a low surface energy functionalized surface on a substrate comprises a mixture of silanes.
DERWENT CLASS: A96 B04 D16 E11 P42
INVENTOR(S): **DELLINGER, D J**; FULCRAND, G; HOTZ, C Z; **LEFKOWITZ, S M**
PATENT ASSIGNEE(S): (DELL-I) DELLINGER D J; (FULC-I) FULCRAND G; (HOTZ-I) HOTZ C Z; (LEFK-I) LEFKOWITZ S M; (AGIL-N) AGILENT TECHNOLOGIES INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001051221	A1	20011213	(200236)*		12
US 6444268	B2	20020903	(200266)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2001051221	A1	Div ex	US 1998-145015	19980901
			US 2001-897340	20010702
US 6444268	B2	Div ex	US 1998-145015	19980901
			US 2001-897340	20010702

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2001051221	A1	Div ex	US 6258454
US 6444268	B2	Div ex	US 6258454

PRIORITY APPLN. INFO: US 1998-145015 19980901; US 2001-897340 20010702

AB US2001051221 A UPAB: 20021014
NOVELTY - A derivatizing composition comprises a mixture of a first and a second silane.
DETAILED DESCRIPTION - A derivatizing composition comprises a first silane of formula R1-Si(RtRxRy) (I) and a second silane R2-(L)n-Si(RtRxRy) (II).
Rt = leaving group;
Rx and Ry = lower alkyl or leaving group;

R1 = a chemically inert group;
n = 0 or 1;
L = a linking group; and
R2 = a functional group.

The functional group enables covalent binding of a molecular group or a modifiable group that can be converted to such a functional group.

INDEPENDENT CLAIMS are also included for the following:

(1) preparation of a low surface energy functionalized surface on a substrate involving contacting a substrate with the derivatizing composition to couple (I) and (II) to the substrate surface and form -Si-R1 (III) and -Si-(L)n-R2 (IV) groups. The substrate has reactive hydrophilic groups (A) on their surface;

(2) preparation of a support-bound cleavable ligands on the low surface energy substrate involving contacting the substrate with the derivatizing composition to couple (I) and (II) to substrate surface to form (III) and (IV), and coupling a ligand to the functional or the modifiable groups through a linking group containing a chemically cleavable site; and

(3) a substrate comprising the solid support having several surface hydrophilic, nucleophilic groups (B).

A first fraction of (B) is covalently bound to (III) and a second fraction of (B) is covalently bound to (IV). The solid support comprises a material selected from polystyrene, agarose, dextran, cellulosic polymers, polyacrylamide or glass.

USE - For preparing the low surface energy functionalized surface on the substrate (claimed); in the field of solid phase chemical synthesis, particularly solid phase synthesis of oligomer arrays.

ADVANTAGE - The composition upon binding to the substrate reduces its surface energy and provides means for covalently binding molecular groups to the substrate surface. The composition significantly reduces spot diameter for a droplet of a given volume. The chemically inert group upon binding to a substrate lowers the surface energy.

Dwg.1/4

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FILE LAST UPDATED: 7 Nov 2002  (20021107/ED)

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=> d que l26; d que l29; d que l32

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L2          9384 SEA FILE=CAPLUS ABB=ON  MICROARRAY?
L3          1621 SEA FILE=CAPLUS ABB=ON  BIOCHIP?
L4           287 SEA FILE=CAPLUS ABB=ON  LAB-ON-A-CHIP/CT
L5        313698 SEA FILE=CAPLUS ABB=ON  LIGAND#
L15       205653 SEA FILE=CAPLUS ABB=ON  ?OLEFIN?
L19        80069 SEA FILE=CAPLUS ABB=ON  NUCLEIC ACID#/CW
L20       597497 SEA FILE=CAPLUS ABB=ON  PROTEINS/CT
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                 OR (L19 OR L20 OR L21) OR (L24 OR L25))



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L3          1621 SEA FILE=CAPLUS ABB=ON  BIOCHIP?
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               (L24 OR L25)) AND (L1 OR L2 OR L3 OR L4)


L1        1148 SEA FILE=CAPLUS ABB=ON  DNA(2A)(CHIP? OR MICROCHIP?)
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L5      313698 SEA FILE=CAPLUS ABB=ON  LIGAND#
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L21     101627 SEA FILE=CAPLUS ABB=ON  PEPTIDES/CT
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L32          5 SEA FILE=CAPLUS ABB=ON  L31 AND DEV/RL
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\ Role Dev = Device Component Use

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L159        14 (L26 OR L29 OR L32) NOT L155
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=> d que 159;d que 168; d que 170

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L52     131506 SEA FILE=WPIDS ABB=ON  ?PEPTIDE? OR PROTEIN#
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L49       2500 SEA FILE=WPIDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?
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L52     131506 SEA FILE=WPIDS ABB=ON  ?PEPTIDE? OR PROTEIN#
L53      20707 SEA FILE=WPIDS ABB=ON  LIGAND#
L55       4514 SEA FILE=WPIDS ABB=ON  BENZALDEHYDE# OR BENZ ALDEHYDE#
L56       1623 SEA FILE=WPIDS ABB=ON  CARBOXYLATE ESTER#
L57     131286 SEA FILE=WPIDS ABB=ON  AMINE#
L58         75 SEA FILE=WPIDS ABB=ON  IMIDAZOL?(2A)CARBAMATE#
L63     113160 SEA FILE=WPIDS ABB=ON  FUNCTIONAL
L66       5558 SEA FILE=WPIDS ABB=ON  (L55 OR L56 OR L57 OR L58)(L)L63
L68          5 SEA FILE=WPIDS ABB=ON  L66 AND (L51 OR L52 OR L53) AND L49


L49       2500 SEA FILE=WPIDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?
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L51      54483 SEA FILE=WPIDS ABB=ON  ?NUCLEOTIDE? OR ?NUCLEIC ACID#
L52     131506 SEA FILE=WPIDS ABB=ON  ?PEPTIDE? OR PROTEIN#
L53      20707 SEA FILE=WPIDS ABB=ON  LIGAND#
L55       4514 SEA FILE=WPIDS ABB=ON  BENZALDEHYDE# OR BENZ ALDEHYDE#
L56       1623 SEA FILE=WPIDS ABB=ON  CARBOXYLATE ESTER#
L57     131286 SEA FILE=WPIDS ABB=ON  AMINE#
L58         75 SEA FILE=WPIDS ABB=ON  IMIDAZOL?(2A)CARBAMATE#
L61    1541619 SEA FILE=WPIDS ABB=ON  DIFFERENT OR SEPARAT? OR MULTIPLE
L70          4 SEA FILE=WPIDS ABB=ON  L61(5A)(L51 OR L52 OR L53) AND L49 AND
               (L55 OR L56 OR L57 OR L58)


=> s (l59 or l68 or l70) not l156

L160        13 (L59 OR L68 OR L70) NOT L156

=> fil biosis; d que 186; d que l88

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 7 November 2002 (20021107/ED)


L78       5511 SEA FILE=BIOSIS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
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L80     113855 SEA FILE=BIOSIS ABB=ON  LIGAND#
L81    1692725 SEA FILE=BIOSIS ABB=ON  ?PEPTIDE? OR PROTEIN#
L82     312924 SEA FILE=BIOSIS ABB=ON  ?NUCLEOTIDE? OR ?NUCLEIC ACID#
L83       4041 SEA FILE=BIOSIS ABB=ON  ?OLEFIN?
L86          0 SEA FILE=BIOSIS ABB=ON  L78 AND (L80 OR L81 OR L82) AND L83


L78       5511 SEA FILE=BIOSIS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
               BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L80     113855 SEA FILE=BIOSIS ABB=ON  LIGAND#
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previously printed

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L81      1692725 SEA FILE=BIOSIS ABB=ON  ?PEPTIDE? OR PROTEIN#
L82       312924 SEA FILE=BIOSIS ABB=ON  ?NUCLEOTIDE? OR ?NUCLEIC ACID#
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L87           10 SEA FILE=BIOSIS ABB=ON  L78 AND (L80 OR L81 OR L82) AND L84
L88            8 SEA FILE=BIOSIS ABB=ON  L87 NOT (MINOXIDIL OR METHAMPHETAMINE)/
                 TI


=> s l88 not l157

L161           8 L88 NOT L157

=> fil jic; d que l103; d que l107; d que l113

FILE 'JICST-EPLUS' ENTERED AT 10:15:51 ON 08 NOV 2002
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L95            443 SEA FILE=JICST-EPLUS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                 BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L97         38346 SEA FILE=JICST-EPLUS ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE#
                 OR POLYNUCLEOTIDE#
L98        323275 SEA FILE=JICST-EPLUS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                 PROTEIN#
L99        128521 SEA FILE=JICST-EPLUS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
                 RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L100        15020 SEA FILE=JICST-EPLUS ABB=ON  LIGAND#
L101       150078 SEA FILE=JICST-EPLUS ABB=ON  OLEFIN? OR POLYOLEFIN?
L103            6 SEA FILE=JICST-EPLUS ABB=ON  L95 AND (L97 OR L98 OR L99 OR
                 L100) AND L101


L95            443 SEA FILE=JICST-EPLUS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                 BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L97         38346 SEA FILE=JICST-EPLUS ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE#
                 OR POLYNUCLEOTIDE#
L98        323275 SEA FILE=JICST-EPLUS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                 PROTEIN#
L99        128521 SEA FILE=JICST-EPLUS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
                 RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L100        15020 SEA FILE=JICST-EPLUS ABB=ON  LIGAND#
L102       245494 SEA FILE=JICST-EPLUS ABB=ON  BENZALDEHYDE# OR CARBOXYLATE
                 ESTER# OR AMINE# OR IMIDAZOL?(2A)CARBAMATE#
L105       102010 SEA FILE=JICST-EPLUS ABB=ON  FUNCTIONAL
L107            3 SEA FILE=JICST-EPLUS ABB=ON  L95 AND (L97 OR L98 OR L99 OR
                 L100) AND L102 AND L105


L95            443 SEA FILE=JICST-EPLUS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                 BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L97         38346 SEA FILE=JICST-EPLUS ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE#
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L98        323275 SEA FILE=JICST-EPLUS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                 PROTEIN#
L99        128521 SEA FILE=JICST-EPLUS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
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              RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L100       15020 SEA FILE=JICST-EPLUS ABB=ON  LIGAND#
L102      245494 SEA FILE=JICST-EPLUS ABB=ON  BENZALDEHYDE# OR CARBOXYLATE
              ESTER# OR AMINE# OR IMIDAZOL?(2A)CARBAMATE#
L113           1 SEA FILE=JICST-EPLUS ABB=ON  L95(S)(L97 OR L98 OR L99 OR
              L100)(S)L102

=> s l103 or l107 or l113

L162          10 L103 OR L107 OR L113

=> fil biotechno; d que l129; d que l133

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     /CT AND BASIC INDEX  <<<


L120        3621 SEA FILE=BIOTECHNO ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
              BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L123      161772 SEA FILE=BIOTECHNO ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE# OR
              POLYNUCLEOTIDE#
L124      612281 SEA FILE=BIOTECHNO ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
              PROTEIN#
L125      460301 SEA FILE=BIOTECHNO ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
              RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L126       47920 SEA FILE=BIOTECHNO ABB=ON  LIGAND#
L127         230 SEA FILE=BIOTECHNO ABB=ON  OLEFIN# OR POLYOLEFIN#
L129           0 SEA FILE=BIOTECHNO ABB=ON  L120 AND (L123 OR L124 OR L125 OR
              L126) AND L127



L120        3621 SEA FILE=BIOTECHNO ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
              BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L123      161772 SEA FILE=BIOTECHNO ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE# OR
              POLYNUCLEOTIDE#
L124      612281 SEA FILE=BIOTECHNO ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
              PROTEIN#
L125      460301 SEA FILE=BIOTECHNO ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
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L126       47920 SEA FILE=BIOTECHNO ABB=ON  LIGAND#
L128        7063 SEA FILE=BIOTECHNO ABB=ON  BENZALDEHYDE# OR CARBOXYLATE ESTER#
              OR AMINE# OR IMIDAZOL?(2A)CARBAMATE#
L130          11 SEA FILE=BIOTECHNO ABB=ON  L120 AND (L123 OR L124 OR L125 OR
              L126) AND L128
L133           4 SEA FILE=BIOTECHNO ABB=ON  L130 AND (FABRICATION OR MANUFACTURE
               OR ATTACHMENT OR PRIMERS)/TI


=> s l133 not l122

L163           4 L133 NOT L122
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previously printed

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=> fil biotechds; d que l149; d que l152; d que l154

FILE 'BIOTECHDS' ENTERED AT 10:15:59 ON 08 NOV 2002
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L141       2598 SEA FILE=BIOTECHDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
L143      29088 SEA FILE=BIOTECHDS ABB=ON  NUCLEOTIDE# OR OLIGONUCLEOTIDE# OR
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L144     102954 SEA FILE=BIOTECHDS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                PROTEIN#
L145      94133 SEA FILE=BIOTECHDS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
                RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L146       5196 SEA FILE=BIOTECHDS ABB=ON  LIGAND#
L147       9495 SEA FILE=BIOTECHDS ABB=ON  OLEFIN# OR POLYOLEFIN#
L149          3 SEA FILE=BIOTECHDS ABB=ON  L141 AND (L143 OR L144 OR L145 OR
                L146) AND L147
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L141       2598 SEA FILE=BIOTECHDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
                BIOCHIP? OR BIO CHIP? OR DNA(2A)(CHIP? OR MICROCHIP?)
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L144     102954 SEA FILE=BIOTECHDS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                PROTEIN#
L145      94133 SEA FILE=BIOTECHDS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
                RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L146       5196 SEA FILE=BIOTECHDS ABB=ON  LIGAND#
L148       4962 SEA FILE=BIOTECHDS ABB=ON  BENZALDEHYDE# OR CARBOXYLATE ESTER#
                OR AMINE# OR IMIDAZOL?(2A)CARBAMATE#
L151       8488 SEA FILE=BIOTECHDS ABB=ON  FUNCTIONAL
L152          3 SEA FILE=BIOTECHDS ABB=ON  L141 AND (L143 OR L144 OR L145 OR
                L146) AND L148 AND L151
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L141       2598 SEA FILE=BIOTECHDS ABB=ON  MICROARRAY? OR MICRO ARRAY? OR
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L144     102954 SEA FILE=BIOTECHDS ABB=ON  POLYPEPTIDE# OR PEPTIDE# OR
                PROTEIN#
L145      94133 SEA FILE=BIOTECHDS ABB=ON  (NUCLEIC OR DEOXYRIBONUCLEIC OR
                RIBONUCLEIC)(W)ACID# OR DNA OR RNA
L146       5196 SEA FILE=BIOTECHDS ABB=ON  LIGAND#
L148       4962 SEA FILE=BIOTECHDS ABB=ON  BENZALDEHYDE# OR CARBOXYLATE ESTER#
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L153      11803 SEA FILE=BIOTECHDS ABB=ON  (L143 OR L144 OR L145 OR L146)(10A)(
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L154          6 SEA FILE=BIOTECHDS ABB=ON  L141 AND L153 AND L148
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=> s (l149 or l152 or l154) not l142
L164         11 (L149 OR L152 OR L154) NOT L142
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previously printed

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=> dup l162,l159,l163,l161,l164,l160
ENTER REMOVE, IDENTIFY, ONLY, OR (?):rem
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PROCESSING COMPLETED FOR L162
PROCESSING COMPLETED FOR L159
PROCESSING COMPLETED FOR L163
PROCESSING COMPLETED FOR L161
PROCESSING COMPLETED FOR L164
PROCESSING COMPLETED FOR L160
L165 53 DUP REM L162 L159 L163 L161 L164 L160 (7 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE JICST-EPLUS
ANSWERS '11-24' FROM FILE CAPLUS
ANSWERS '25-28' FROM FILE BIOTECHNO
ANSWERS '29-32' FROM FILE BIOSIS
ANSWERS '33-43' FROM FILE BIOTECHDS
ANSWERS '44-53' FROM FILE WPIDS

=> d ibib ab 1-53; fil hom

L165 ANSWER 1 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020361640 JICST-EPlus
TITLE: Studies on the Antimicrobial Mechanisms of Capsaicin Using Yeast **DNA Microarray**.
AUTHOR: KURITA S; KITAGAWA E; KIM C-H; MOMOSE Y; IWAHASHI H
CORPORATE SOURCE: National Inst. Advanced Industrial Sci. And Technol., Ibaraki, Jpn
SOURCE: Biosci Biotechnol Biochem, (2002) vol. 66, no. 3, pp. 532-536. Journal Code: G0021A (Fig. 2, Tbl. 1, Ref. 18)
CODEN: BBBIEJ; ISSN: 0916-8451
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB Capsaicin is a pungent element in a variety of red peppers that are widely used as food additives and considered to be an antimicrobial factor. For our tests, we used yeast **DNA micro-array** methods to understand the mechanisms of inhibitory effects of capsaicin. The capsaicin treatment significantly induced 39 genes from approximately 6,000 genes. These induced genes were classified as multi-drug resistance transporter genes, membrane biosynthesis genes, genes encoding stress **proteins**, and uncharacterized genes. The growth abilities of the strains with the deletion of the induced genes suggest that capsaicin is pumped out of the yeast cells by the PDR5 transporter. (author abst.)

L165 ANSWER 2 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020616832 JICST-EPlus
TITLE: **DNA Microarray** Fabrication by

Photo-Sensitive Polyvinyl Alcohol.
AUTHOR: NAKAUCHI G; OHTANI Y; INAKI Y; MIYATA M
CORPORATE SOURCE: Osaka Univ., Osaka, Jpn
SOURCE: J Photopolym Sci Technol, (2002) vol. 15, no. 1, pp. 109-110. Journal Code: L0202A (Fig. 5, Ref. 3)
CODEN: JSTEEW; ISSN: 0914-9244
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Short Communication
LANGUAGE: English
STATUS: New

L165 ANSWER 3 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020493371 JICST-EPlus
TITLE: The Analysis of the Intracellular Vesicular Transport.
AUTHOR: YOSHIZAWA AKIYASU
CORPORATE SOURCE: Kyodai Kaken Baioinfomatikususe
SOURCE: Supakonpyuta Raboratori. Heisei 13 Nendo. Kenkyu Seika Hokokusho, (2002) pp. 80-82. Journal Code: N20020944 (Fig. 3, Ref. 4)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB **Protein-protein** interaction data (I) from the study on budding Saccharomyces cerevisiae and **protein** by two-hybrid method and co-expression data (II) in budding yeast by **Microarray** method were analyzed to clarify the relationship among the genes involved in intracellular transport. A total of 1547 genes were included both in dataset I and II, and gene-gene relation commonly found in both datasets was only one. There were 12 clusters that include a gene related to the transport of vesicle. **Protein** YIL177 was an unknown **functional protein** and related to three clusters, suggesting that the **protein** might be involved in the transport of vesicle.

L165 ANSWER 4 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020472872 JICST-EPlus
TITLE: The induction of ADRG#34 after chromic antidepressant treatment and repeated electroconvlusive treatment in rat brain.
AUTHOR: YAMADA MITSUHIKO
KAMIJIMA KUNITOSHI
HIGUCHI TERUHIKO
CORPORATE SOURCE: Showadai Karasuyamabyoin Seishin'igaku
Showadai I Seishin'igaku
Kokuritsu Seishin Shinkei Senta Konodai Byoin
SOURCE: Seishin Yakuryo Kenkyu Nenpo (Annual Report of the Pharmacopsychiatry Research Foundation), (2002) no. 34, pp. 45-51. Journal Code: Y0939A (Fig. 6, Ref. 6)
ISSN: 0286-7591
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB Previously, we have identified 200 cDNA fragments as antidepressant related genes/ESTs (ADRG#1-200). In this study, using these cDNAs, we developed our original cDNA **microarray** for rapid secondary screening of candidate genes as the novel therapeutic targets. With this **microarray**, we found that the expression of a novel gene, ADRG#34, was significantly increased in rat frontal cortex after chronic antidepressant treatment and repeated electroconvulsive treatment(ECT), another therapeutic treatment of depression. RT-PCR analysis also demonstrated the induction of ADRG#34 at mRNA levels in rat frontal cortex

after these treatment. On the other hand, single administration had no effect on ADRG#34 expression. We then determined the full length of ADRG#34 encoded 685 amino acid residues containing a RING-H2 finger motif at the carboxy-terminal. Our data suggest that ADRG#34 may be one of the common **functional** molecules induced after chronic antidepressant treatment and ECT. Our results may contribute to a novel model for the therapeutic mechanism of depression and new molecular targets for the development of therapeutic agents. (author abst.)

L165 ANSWER 5 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020079995 JICST-EPlus
TITLE: Single Nucleotide Polymorphism Analysis Using a Bacterial Magnetic Particle Microarray.
AUTHOR: YOSHINO T; TAKEYAMA H; MATSUNAGA T
CORPORATE SOURCE: Tokyo Univ. Agriculture And Technol., Tokyo, Jpn
SOURCE: Denki Kagaku oyobi Kogyo Butsuri Kagaku, (2001) vol. 69, no. 12, pp. 1008-1012. Journal Code: G0072A (Fig. 6, Tbl. 2, Ref. 17)
ISSN: 1344-3542
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB An approach to analyzing single **nucleotide** polymorphism (SNP) found in the human genome has been developed using a bacterial magnetic particle (BMP) **microarray**. Streptavidin was bound to BMPs using biotin labeled cross-linkers reacting with the **amine** group on BMPs. PCR was performed using TRITC and biotin labeled primer pairs for amplification of ALDH2 fragment. PCR products were conjugated with BMPs by the interactions of biotin-streptavidin. **DNA**-BMP complexes were spotted on a slide-glass, immobilized magnetically then treated with a restriction enzyme specifically digesting the wild-type sequences (normal allele of ALDH2). The homozygous (ALDH2*1/*1), heterozygous (ALDH2*1/*2), and mutant (ALDH2*2/*2) genotypes were successfully discriminated by imaging the BMP **microarray** before and after digestion and measuring spot fluorescence intensities on the slide glass. (author abst.)

L165 ANSWER 6 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1020332155 JICST-EPlus
TITLE: Analysis of Gene Expression Profiles Associated with Cisplatin Resistance in Human Ovarian Cancer Cell Lines and Tissues Using cDNA **Microarray**.
AUTHOR: SAKAMOTO M; KONDO A; KAWASAKI K; GOTO T; TENJIN Y
SAKAMOTO H
OCHIAI K; TANAKA T
KIKUCHI Y
CORPORATE SOURCE: Sasaki Inst. Kyoundo Hospital
National Defense Medical Coll.
Jikei Univ. School Of Medicine
Olympus
SOURCE: Human Cell, (2001) vol. 14, no. 4, pp. 305-315. Journal Code: L0042A (Fig. 7, Tbl. 5, Ref. 21)
ISSN: 0914-7470
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB Gene expression profiles were analyzed by using cDNA **microarray** for a cisplatin-sensitive cell line (KF), and three- and thirty- fold cisplatin-resistant ovarian cancer cell lines (KFr and KFrP200) both showing no p53 mutation within exon 5,6,7,8 and no p-glycoprotein overexpression. Expression of GST-pi mRNA increased as the level of resistance to cisplatin became high. **Microarray** analysis

revealed that **DNA** repair associated genes, i.e., XRCC5, XRCC6, ERCC5, hMLH1 were over-expressed in three-fold cisplatin-resistant cell line, KFr as compared to cisplatin-sensitive parental cell line, KF. Apoptosis inhibitors, i.e., IGFR type I and II were over-expressed, and apoptosis inducer, i.e., caspase 3 and BAK were underexpressed in highly cisplatin-resistant cell line, KFrP200 as compared to KFr. As for clinical cases, cDNA **microarray** was used to compare gene expression profiles directly between two groups, i.e., the chemotherapy (CAP) sensitive group (n=2) and the resistant group (n=2). Six genes such as beta tubulin, high-mobility group (nonhistone chromosomal) **protein** 1, connective tissue growth factor, insulin-like growth factor binding **protein** 2, alpha tubulin, and RAS-related gene were overexpressed in CAP therapy resistance group, whereas seven genes such as CD9 antigen, alpha-2-macroglobulin, caveolin 2, interleukin 1 receptor antagonist, Rho GTPase activating **protein** 1, reticulon 3, cyclin-dependent kinase 10, keratin 7 were underexpressed in CAP therapy resistance group. By increasing clinical case number and gene number of **microarray** to be used in the analysis of expression profile of gene cluster affecting anticancer drug resistance and sensitivity of the ovarian cancer, it would be possible to apply **microarray** analysis to personalization of chemotherapy such as selection of effective chemotherapy protocol and prediction of therapeutic effect in the near future. (author abst.)

L165 ANSWER 7 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1010394588 JICST-EPlus
TITLE: **DNA microarray** analysis of hypertrophic change in cardiac myocytes.
AUTHOR: UENO S; IKEDA U; SHIMADA K; MANO H
CORPORATE SOURCE: Jichi Medical School, Tochigi, Jpn
SOURCE: Jpn Circ J, (2001) vol. 65, no. Supplement 1-A, pp. 160. Journal Code: F0908A
CODEN: NJUGAK; ISSN: 0047-1828
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Preprint
LANGUAGE: English
STATUS: New

L165 ANSWER 8 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1010739797 JICST-EPlus
TITLE: Detection of the Retinoic Acid-regulated Genes in a RTBM1 Neuroblastoma Cell Line Using cDNA **Microarray**.
AUTHOR: UEDA K
CORPORATE SOURCE: Kurume Univ. School Of Medicine, Kurume, Jpn
SOURCE: Kurume Med J, (2001) vol. 48, no. 2, pp. 159-164. Journal Code: F0811A (Fig. 4, Tbl. 1, Ref. 31)
CODEN: KRMJAC; ISSN: 0023-5679
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
AB A **microarray** system is a powerful and very useful technology for analyzing the expression profile of thousands of genes. In this study, we made a cDNA **microarray** system carrying 2007 cDNAs obtained from primary neuroblastoma cDNA library and identified retinoic acid (RA)-regulated genes in a RTBM1 neuroblastoma cell line. We repeated independent hybridization experiment twice and found that 7 genes were up-regulated, and 5 genes were down-regulated on the cDNA **microarray**. The semi-quantitative reverse transcriptase (RT)-PCR analysis to confirm the results showed that 4 genes which included amyloid precursor-like **protein** 2 (APLP2), P311, dihydropyrimidinase related **protein3** (DRP3) and RGP4 were up-regulated, while 2 genes. Id-2 and vimentin, were down-regulated. Thus, our neuroblastoma cDNA **microarray** system is useful to screen the neuronal

difterentiation- and growth-related genes regulated by RA with high efficiency. (author abst.)

L165 ANSWER 9 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1010614477 JICST-EPlus
TITLE: A **DNA microarray** analsis for the effect of spermatogenesis to phytoestrogen and endocrine disruptors in mice.
AUTHOR: ADACHI TETSUYA; SAKURAI KEN'ICHI; KOMIYAMA MASATOSHI; SHIBAYAMA TAKAKO; MORI CHISATO
FUKATA HIDEKI
IGUCHI TAISEN
CORPORATE SOURCE: Chibadai I Kaibougakudaiichikoza
Fukadaseimeikagakuken
Okazakikokuritsukyodokiko Kisoseibutsugakuken
SOURCE: Chiba Igaku Zasshi (Chiba Medical Journal), (2001) vol. 77, no. 3, pp. 151-158. Journal Code: G0640A (Fig. 4, Tbl. 3, Ref. 23)
CODEN: CIZAAZ; ISSN: 0303-5476
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB In this study, we examined the effect of neonatal exposure of genistein (Gen), diethylstilbestrol (DES) or bisphenol A (BPA), known as endocrine disruptors on testicular gene expression, using **DNA microarray** analysis. Male ICR mice, 1 day after birth, were used, and the mice were exposed to Gen (1mg/mouse/day), DES (50.MU.g/mouse/day) or BPA (0.2mg/mouse/day) for 5 days. The testicular **RNA** of 3-month-old mice was prepared, and the difference between the exposed and the nonexposed group of endocrine disruptors was determined using the **DNA microarray** method. The genes whose expression was changed with administration of Gen, DES or BPA are number 38, 34 and 12, respectively, in 8800 genes. Our results suggest that **DNA** microarry analysis is useful method by which a large number of the gene expression changes are simultaneously detected, and that neonatal exposure of endocrine disruptors causes a number of changes in gene expression in the testes of adult mice. (author abst.)

L165 ANSWER 10 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1001038337 JICST-EPlus
TITLE: Study on Cancer Preventive Substances in Soybeans.
AUTHOR: NISHINO HOYOKU
CORPORATE SOURCE: Kyoto Prefect. Univ. of Med.
SOURCE: Daizu Tanpakushitsu Kenkyu (Soy Protein Research), (2000) vol. 3, pp. 59-62. Journal Code: L0927B (Fig. 2, Tbl. 3, Ref. 1)
CODEN: DTKEFV; ISSN: 1344-4050
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB In the previous study, we showed that genistein, one of the isoflavonoids found in soybean, inhibited the proliferation of prostate cancer DU145 cells. In addition to prostate cancer cells, various tumor cell lines were also proven to be sensitive to genistein. In the present study, we confirmed that genistein has anti-proliferative activity on human tumor cells, including gastric cancer cell line and lung cancer cell lines. Thus, genistein seems to be useful for the cancer control in a wide range spectrum. Further analysis of action mechanism of genistein is important before starting new clinical intervention trials, because of the development of novel methods, such as **DNA** array technology and proteomics technology, has recently been achieved. In this context, we

evaluated the potency of genistein on expression of wide variety of genes using **DNA** macroarray, and found that the treatment of DU145 cells with genistein resulted in early induction of cell cycle related genes, such as p53, p53-dependent cell growth regulator CGR19, MDM2-like p53-binding **protein**, RBQ-3 and so on. We are now extending this kind of study by means of **DNA microarray**. And introduction of proteomics is now in planning. Since various substances co-exist with isoflavonoids in soybean, studies on these soybean constituents seem to be also valuable. Thus, we have started to assess biological activities of these substances, including soyasaponins, tocotrienol, and phytic acid. In the present study, we confirmed anti-tumor promoter activity of soyasaponin I and II. (author abst.)

L165 ANSWER 11 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:51671 CAPLUS
DOCUMENT NUMBER: 136:80848
TITLE: Method for detecting sequence variation of nucleic acids using PCR with allele-specific primers
INVENTOR(S): Jang, Gi Young
PATENT ASSIGNEE(S): Bionex, Inc., S. Korea
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004673	A1	20020117	WO 2000-KR753	20000712
W: AU, BR, CA, CN, ID, IL, IN, JP, KR, MX, NZ, RU, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 2000057122	A5	20020121	AU 2000-57122	20000712

PRIORITY APPLN. INFO.: WO 2000-KR753 A 20000712

AB The present invention provides a simple and convenient method for detection of sequence variation of nucleic acid. It involves a PCR amplification process with 2 or more oligonucleotide primers that preferably have their 3' end complementary to predetd. variants of the nucleic acid. Each primer carries **different** kinds of detectable markers like fluorescent dyes, radioisotopes, digoxigenin, Cyber green or biotin. The oligonucleotides are competitively hybridized to the nucleic acid and extended. To differentiate between hybridization of perfectly matched and unmatched oligonucleotides, hybridization temp. is gradually decreased. After the extension with DNA polymerase, the extension products are detected by their resp. labels. A nucleic acid which may carry a sequence variation is immobilized to a solid material such as a glass plate, membrane or magnetic bead. The nucleic acid can be prepd. by cutting cloned DNA with a restriction enzyme and could also be part of a larger DNA such as a plasmid or a genome. Next, two or more **different** oligonucleotides which are complementary to the nucleic acid are added. The oligonucleotides are uniform in length (7-20 nucleotides). The 5'-ends of the primers are labeled with **different** detectable markers and the 3'-ends have sequences complementary to two or more **different** predetd. sequence variants of the nucleic acid. Two oligonucleotides are selected from normal unmodified oligonucleotide primers, 5' biotin-labeled oligonucleotide primers and 5' **amine**-labeled oligonucleotide primers. The nucleic acid is denatured by heating. Next, the oligonucleotides are hybridized to the nucleic acid and extending using thermostable DNA polymerase by gradually decreasing the temp. (0.01 to 3.degree./s or 0.1 to 4.degree./s). The extension reaction contains a mixt. of dATP, dGTP, dCTP and biotin-labeled dUTP. The extended nucleic

acid product is detected using DNA sequencing anal., gel scanning technol. or **microarrays**. A method of detecting sequence variations of nucleic acid carrying plural sequence variations is provided. A method of detecting sequence variations of a double-stranded nucleic acid using two or more **different** universal oligonucleotides which are not complementary to any part of the nucleic acid sequence, adding two or more primers with 5' end having same sequence to universal oligonucleotide and 3' end having sequence complementary to predetd. sequence variants, and adding std. PCR oligonucleotides complementary to the nucleic acid.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:618201 CAPLUS
DOCUMENT NUMBER: 135:177677
TITLE: Smooth-surfaced porous membranes and composite membranes for assay devices and test kits
INVENTOR(S): Salinaro, Richard F.; Rothman, Isaac; Gsell, Thomas C.
PATENT ASSIGNEE(S): Pall Corporation, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061042	A2	20010823	WO 2001-US4974	20010216
WO 2001061042	A3	20020207		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-183327P P 20000218
US 2000-220825P P 20000726

AB Disclosed are smooth-surfaced porous membranes having one or more advantages such as low autofluorescence, thermal-cyclability, esp. under humid conditions, and three-dimensional binding capacity. The membrane can be free-standing or, preferably in combination with a support as in a composite membrane. The present invention provides a composite membrane comprising a porous polymer layer disposed on a support. The present invention further provides devices such as **microarray** devices comprising the composite for the anal. of biomaterials such as nucleic acids. A composite membrane comprising a nylon 66 layer on a polycarbonate support was prepd. and the surface was analyzed. The composite membrane had a smooth surface profile.

L165 ANSWER 13 OF 53 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 2000:772796 CAPLUS
DOCUMENT NUMBER: 133:346746
TITLE: Hydrogel **biochip** and its preparation from biomolecular probes and hydrogel prepolymers
INVENTOR(S): Hahn, Soonkap; Fagnani, Roberto; Tsinberg, Pavel
PATENT ASSIGNEE(S): Biocept, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000065097	A1	20001102	WO 2000-US11282	20000426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6174683	B1	20010116	US 1999-299831	19990426
EP 1173620	A1	20020123	EP 2000-928450	20000426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-299831 A 19990426
WO 2000-US11282 W 20000426

AB Methods for prepg. a hydrogel **biochip** are disclosed wherein a plurality of biomol. probes are bound to a hydrogel prepolymer either prior to or simultaneously with polymn. of the prepolymer. While either hydrogel is polymg., it is microspotted onto a solid substrate to which the hydrogel becomes covalently bound in the form of a hydrogel microdroplet. Adjustment of the reactivity of the prepolymer and the polymn. conditions provides effective control of the d. of biomol. probe immobilization. Resulting **biochips** contg. a plurality of such microdroplets having **different** biomols. bound thereto are useful for gene discovery, gene characterization, functional gene anal., screening for biol. activity and related studies. Pre-Ma G-50 in 0.33 g acetonitrile and 0.33 g N-methyl-2-pyrrolidinone (34.5 parts) was mixed with various oligonucleotides in 1 mL 50 mM borate buffer at pH 8.0 (65.5 parts). The solns. were microspotted onto a glass slide, the slide was placed into a controlled humidifier chamber for 1 h and then washed to prep. a **biochip**. A fluorescein-labeled target 30-mer DNA from the sequence of the human .beta.-globin gene was tested on the slide. The target could discriminated between a perfect match and one-base-pair mismatch. Non-related oligonucleotides and blank hydrogels gave fluorescent intensities just above background showing min. non-specific binding to the hydrogel.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:716470 CAPLUS
DOCUMENT NUMBER: 137:244246
TITLE: Methods for fabrication of **microarrays** containing polymeric biomaterials for use in high-throughput drug screening and gene expression profiling
INVENTOR(S): Langer, Robert S.; Anderson, Daniel G.; Putnam, David A.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072812	A2	20020919	WO 2002-US6771	20020306
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002142304	A1	20021003	US 2001-803319	20010309

PRIORITY APPLN. INFO.: US 2001-803319 A 20010309

AB A **microarray** of polymeric biomaterials is provided. Specifically, a **microarray** of polymeric biomaterials that comprises a base with a cytophobic surface, and a plurality of discrete polymeric biomaterial elements bound to the cytophobic surface, is provided. Preferably said polymeric biomaterials comprise a synthetic polymer. Said polymeric biomaterials may also comprise other compds. covalently or non-covalently attached to said synthetic polymer. Methods of prepg. the **microarray** of polymeric biomaterials of the present invention and uses of the **microarray** of polymeric biomaterials of the present invention are also provided. The said polymeric biomaterials may be 10-1000 .mu.m in diam. at placed at 100-1200 .mu.m intervals in a rectangular **microarray** at a d. of 1-1000 polymeric biomaterials/cm2 and as drops of between 0.1-100 nl.

L165 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:466288 CAPLUS
DOCUMENT NUMBER: 137:17415
TITLE: Methods, devices, arrays and kits for detecting and analyzing biomolecules
INVENTOR(S): Knezevic, Vladimir; Emmert-Buck, Michael R.; Baibakova, Galina; Hartmann, Dan-Paul; Hewitt, Stephen; Mitchell, Capre; Gardner, Kevin
PATENT ASSIGNEE(S): 20/20 Gene Systems, Inc., USA; The Government of the United States of America, as Represented by the Secretary, Department of Health & Human Services, the National Institutes Of
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002048674	A2	20020620	WO 2001-US44009	20011120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002012920	A1	20020131	US 2001-753574	20010104
AU 2002043236	A5	20020624	AU 2002-43236	20011120

PRIORITY APPLN. INFO.:
US 2000-718990 A 20001120
US 2001-753574 A 20010104
US 2001-286258P P 20010425
US 2001-296475P P 20010608
US 2001-304031P P 20010709
WO 2001-US44009 W 20011120

AB The invention concerns devices, arrays, kits and methods for detecting biomols. in a tissue section (such as a fresh or archival sample, tissue

microarray, or cells harvested by an laser capture microdissection (LCM) procedure) or other substantially two-dimensional sample (such as an electrophoretic gel or cDNA **microarray**) by creating "carbon copies" of the biomols. eluted from the sample and visualizing the biomols. on the copies using one or more detector mols. (e.g., antibodies or DNA probes) having specific affinity for the biomols. of interest. Specific methods are provided for identifying the pattern of biomols. (e.g., proteins and nucleic acids) in the samples. Other specific methods are provided for the identification and anal. of proteins and other biol. mols. produced by cells and/or tissue, esp. human cells and/or tissue. The disclosure also provides a plurality of differentially prepd. and/or processed membranes that can be used in described methods, and which permit the identification and anal. of biomols. Diagrams describing the app. assembly and operation are given.

L165 ANSWER 16 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:172136 CAPLUS
DOCUMENT NUMBER: 136:211857
TITLE: Arrays of immobilized biomolecules and their production
INVENTOR(S): Grill, Hans-Joerg; Prix, Lothar; Schuetz, Andreas
PATENT ASSIGNEE(S): Giesing, Michael, Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018634	A2	20020307	WO 2001-EP9864	20010827
WO 2002018634	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10041809	A1	20020307	DE 2000-10041809	20000825
AU 2002021592	A5	20020313	AU 2002-21592	20010827

PRIORITY APPLN. INFO.: DE 2000-10041809 A 20000825
WO 2001-EP9864 W 20010827

AB The invention relates to arrays of immobilized biomols., coupled by means of coupling groups, preferably quinone, to a carbonaceous support surface. The carbonaceous surface comprises at least one polymer based on **cycloolefins**, or may be obtained whereby a glass, metal or ceramic surface is treated with an aq. soln. of at least one carbon-contg. compd. which may be hydrolyzed and the surface subjected to thermal treatment. Anthraquinone and **polycycloolefin** surfaces based on norbornene are preferably used, or surfaces silanized with hydrophobic residues according to the sol-gel technique. The advantages of the arrays are their gog quality, in particular with relation to the homogeneity and reproducibility with which the biomols. are immobilized. The invention further relates to methods for the immobilization of biomols. and the use of the arrays for diagnostic purposes.

L165 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:755070 CAPLUS
DOCUMENT NUMBER: 137:259612

TITLE: Porous substrates for DNA arrays
INVENTOR(S): Bardhan, Pronob; Bookbinder, Dana C.; Lahiri, Joydeep; Tanner, Cameron W.; Tepesch, Patrick D.; Wusirika, Raja R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S. Ser. No. 650.885, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002142339	A1	20021003	US 2002-101144	20020318

PRIORITY APPLN. INFO.: US 1999-152186P P 19990902
US 2000-650885 B2 20000830

AB A planar, rigid substrate made from a porous, inorg. material coated with cationic polymer mols. for attachment of an array of biomols., such as DNA, RNA, oligonucleotides, peptides, and proteins. The substrate has a top surface with about at least 200 to about 200,000 times greater surface area than that of a comparable, non-porous substrate. The cationic polymer mols. are anchored on the top surface and in the pores of the porous material. In high-d. applications, an array of polynucleotides of a known, predetd. sequence is attached to this cationic polymer layer, such that each of the polynucleotide is attached to a **different** localized area on the top surface. The top surface has a surface area for attaching biomols. of approx. 387,500 cm2/cm"up.degree.2 "up.degree. of area (7.5 million cm2/1.times.3 in. piece of substrate). Each pore of the plurality of pores in the top surface of the substrate has a pore radius of between about 40 .ANG. to about 75 .ANG.. Not only does the cationic coating in and over the pores of the substrate greatly increase the overall pos. charge on the substrate surface, but also given the size of the pores provides binding sites to which biomols. can better attach.

L165 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:444435 CAPLUS
DOCUMENT NUMBER: 137:17395
TITLE: On-spot hydrophilic enhanced slide and preparation thereof
INVENTOR(S): Jan, Bor-Iuan; Tsao, Jia-Hüey; Ho, Chih-Wei; Pan, Chao-Chi; Chow, Zu-Sho; Chang, Yao-Sung; Wu, Cheng-Tao; Kuo, Wen-Hsun
PATENT ASSIGNEE(S): Industrial Technology Research Institute, Taiwan
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403368	B1	20020611	US 2000-695254	20001025
US 2002122875	A1	20020905	US 2002-136357	20020502

PRIORITY APPLN. INFO.: TW 2000-89113659 A 20000710
US 2000-695254 A3 20001025

AB The invention discloses an on-spot hydrophilic enhanced slide/ **microarray**. The prepn. method relates to a hydrophobic copolymer prepd. by blending, grafting or co-polymn. of a hydrophobic material and a compd. bearing functional groups such as anhydride, imide, cyclic amide, and cyclic ester, and application of the hydrophobic copolymer onto an

org. or inorg. substrate. The resulting slide has the properties of on-spot hydrophilic/hydrophobic dynamic conversion, as well as on-spot hydrophilic enhancement for the prepn. of high-d. and high-efficiency bio-chip/**microarray**. Poly(styrene-co-maleic anhydride) was coated onto metallocene **cycloolefine** copolymers substrates at 4,000 rpm. The slides were dried in the oven at 100.degree. to remove solvent. A synthetic oligonucleotide probe Sp5 was immobilized on the slides.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 19 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:148848 CAPLUS
DOCUMENT NUMBER: 136:196593
TITLE: Novel coating resin plate for nucleic acid chip
INVENTOR(S): Hatakeyama, Kazuhisa; Terauchi, Makoto; Saito, Yasuyo
PATENT ASSIGNEE(S): Mitsubishi Chemical Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060671	A2	20020226	JP 2000-244056	20000811

AB A novel coating resin plate is provided, which is suited for efficiently immobilizing a biol. material (e.g., nucleic acid, peptide, protein, antibody) in a stable state, or for being processed to be a chip. The coating resin plate comprises a resin base material (e.g., acrylic resin, styrene resin, polycarbonate resin, **polyolefin** resin) coated with a coating resin (e.g., acrylic resin) possessing at least one or more than one type of functional group selected from a group consisting of a functional group with pos. charges (e.g., quaternary amino group, phosphonium group, sulfonium group, biguanide group, betaine group), a functional group possessing a tertiary amino group (e.g., urethane group, urea group, hydrazide group, amide group, amino group), a functional group capable of forming a covalent bond with an amino group in the biol. material (e.g., alkylcarbonyl group, arylcarbonyl group, formyl group, epoxy group, azlactone group, episulfide group, acryloyl group, methacryloyl group, acrylamide group, methacrylamide group, maleimide group), hydroxyl group, sulfonate group and phosphate group. Alternatively, the coating resin plate comprises the hardened material of this coating resin.

L165 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:331906 CAPLUS
DOCUMENT NUMBER: 136:337313
TITLE: Patterned surfaces for bioconjugation and their preparation
INVENTOR(S): Klapproth, Holger; Wagner, Gerhard
PATENT ASSIGNEE(S): Biochip Technologies G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1202062	A1	20020502	EP 2000-123706	20001031

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
WO 2002037110 A1 20020510 WO 2001-EP12531 20011030
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002012351 A5 20020515 AU 2002-12351 20011030
PRIORITY APPLN. INFO.: EP 2000-123706 A 20001031
WO 2001-EP12531 W 20011030

AB The invention relates to a method for the large scale prodn. of patterned active surfaces for bioconjugation comprising the steps of:(a) prepg. a self-supporting film of a polyfunctional polymer network comprising an assembly of cross-linked polymer subchains, wherein each polymer subchain comprises a multitude of identical or **different** repeating units carrying one or more functional groups which allow an interaction of the polymer with one or more probe mols., (b) providing said self-supporting film with patterned arrays of said one or more probe mols. via an interaction with said functional groups, and (c) fixing said self-supporting film on a solid surface. In a preferred embodiment of the invention the patterned active surface obtained is cut into an endless tape of a desired format and wound up onto a drum. This "endless chip" is ready for fixing to a solid surface of any material or shape. N-methacryloyl-6-aminocapronic acid hydroxysuccinimide ester was prepd. and used to form a polyfunctional polymer network with N,N-dimethylacrylamide, and ethylene glycol bismethacrylate. The polymer network was fixed to a microscope slide covered with a layer of benzophenone-based bifunctional silane linker. A 5-amino-modified oligonucleotide was printed onto the polymer network and coupled to the surface to make a sensor.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:598434 CAPLUS
DOCUMENT NUMBER: 135:177719
TITLE: Target molecule attachment to surfaces
INVENTOR(S): Chappa, Ralph A.; Hu, Sheau-Ping; Swan, Dale G.; Swanson, Melvin J.; Guire, Patrick E.
PATENT ASSIGNEE(S): Surmodics, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. 5,858,653.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001014448	A1	20010816	US 1999-227913	19990108
US 6465178	B2	20021015		
US 5858653	A	19990112	US 1997-940213	19970930
WO 2000040593	A2	20000713	WO 2000-US535	20000110
WO 2000040593	A3	20001228		

W: AU, CA, JP, MX
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 1141385 A2 20011010 EP 2000-903199 20000110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002534663 T2 20021015 JP 2000-592301 20000110
PRIORITY APPLN. INFO.: US 1997-940213 A2 19970930
US 1999-227913 A 19990108
WO 2000-US535 W 20000110

AB Method and reagent compn. for covalent attachment of target mols., such as nucleic acids, onto the surface of a substrate are described. The reagent compn. includes groups capable of covalently binding to the target mol. Optionally, the compn. can contain photoreactive groups for use in attaching the reagent compn. to the surface. The reagent compn. can be used to provide activated slides for use in prepg. **microarrays** of nucleic acids. Glass slides coated with a copolymer of acrylamide, N-[3-(4-benzoylbenzamido)propyl]methacrylamide (BBA-APMA), and N-succinimidyl 6-maleimidohexanoate (MAL-EAC-NOS) (prepn. given) were reacted with amine-modified PCR products from the .beta.-galactosidase gene using **microarraying** spotting pins.

L165 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:67423 CAPLUS
DOCUMENT NUMBER: 132:119544
TITLE: Matrices with memories and uses thereof
INVENTOR(S): Nova, Michael P.; Parandoosh, Zahra; Senyei, Andrew E.; Xiao, Xiao-Yi; David, Gary S.; Satoda, Yozo; Zhao, Chanfeng; Potash, Hanan
PATENT ASSIGNEE(S): Irori, USA
SOURCE: U.S., 113 pp., Cont.-in-part of U.S. Ser. No. 711,426.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6017496	A	20000125	US 1996-709435	19960906
US 5741462	A	19980421	US 1995-428662	19950425
US 5925562	A	19990720	US 1995-480196	19950607
US 6331273	B1	20011218	US 1995-473660	19950607
US 6352854	B1	20020305	US 1995-480147	19950607
US 6416714	B1	20020709	US 1995-484486	19950607
US 5874214	A	19990223	US 1995-538387	19951003
US 6025129	A	20000215	US 1995-567746	19951205
WO 9636436	A1	19961121	WO 1996-US6145	19960425
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 6319668	B1	20011120	US 1996-669252	19960624
US 6284459	B1	20010904	US 1996-711426	19960905
US 5961923	A	19991005	US 1996-723423	19960930
WO 9712680	A2	19970410	WO 1996-US15999	19961003
WO 9712680	A3	19970821		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				

AU 9672573		A1	19970428	AU 1996-72573	19961003
EP 853497		A2	19980722	EP 1996-934064	19961003
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
WO 9749653		A2	19971231	WO 1997-US11035	19970624
WO 9749653		A3	19980226		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9735779		A1	19980114	AU 1997-35779	19970624
US 6329139		B1	20011211	US 1997-912998	19970811
US 6340588		B1	20020122	US 1998-51022	19980922

PRIORITY APPLN. INFO.:

US 1995-428662	A2	19950425
US 1995-184504	A2	19950607
US 1995-473660	A2	19950607
US 1995-480147	A2	19950607
US 1995-480196	A2	19950607
US 1995-484486	A2	19950607
US 1995-538387	A2	19951003
US 1995-567746	A2	19951205
US 1996-639813	B2	19960402
WO 1996-US6145	A2	19960425
US 1996-669252	A2	19960624
US 1996-711426	A2	19960905
US 1995-484504	A2	19950607
US 1996-633410	A2	19960610
US 1996-20706P	P	19960624
US 1996-709435	A2	19960906
US 1996-723423	A	19960930
WO 1996-US15999	W	19961003
US 1996-726703	B2	19961007
US 1996-743984	A2	19961028
US 1996-741685	B2	19961031
US 1997-857800	B2	19970122
US 1997-826253	B2	19970327
WO 1997-US11035	W	19970624
US 1997-945053	B2	19971021

AB Combinations, called matrixes with memories, of matrix materials that are encoded with an optically readable code are provided. The matrix materials are those that are used in as supports in solid phase chem. and biochem. syntheses, immunoassays and hybridization reactions. The matrix materials may addnl. include fluorophors or other luminescent moieties to produce luminescing matrixes with memories. The memories include electronic and optical storage media and also include optical memories, such as bar codes and other machine-readable codes. By virtue of this combination, mols. and biol. particles, such as phage and viral particles and cells, that are in proximity or in phys. contact with the matrix combination can be labeled by programming the memory with identifying information and can be identified by retrieving the stored information. Combinations of matrix materials, memories, and linked mols. and biol. materials are also provided. The combinations have a multiplicity of applications, including combinatorial chem., isolation and purifn. of target macromols., capture and detection of macromols. for anal. purposes, selective removal of contaminants, enzymic catalysis, cell sorting, drug delivery, chem. modification and other uses. Methods for tagging mols., biol. particles and matrix support materials, immunoassays, receptor binding assays, scintillation proximity assays, non-radioactive proximity assays, and other methods are also provided. Scintillant-encased glass

beads and chips were prepd. and used in assays.
REFERENCE COUNT: 719 THERE ARE 719 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 23 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:636045 CAPLUS
DOCUMENT NUMBER: 131:269242
TITLE: Matrices with memories and uses thereof
INVENTOR(S): Nova, Michael P.; Parandoosh, Zahra; Senyei, Andrew E.; Xiao, Xiao Yi; David, Gary S.; Satoda, Yozo; Zhao, Chanfeng; Potash, Hanan
PATENT ASSIGNEE(S): Irori, USA
SOURCE: U.S., 119 pp., Cont.-in-part of U.S. Ser. No. 428,662. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5961923	A	19991005	US 1996-723423	19960930
US 5741462	A	19980421	US 1995-428662	19950425
US 5925562	A	19990720	US 1995-480196	19950607
US 6331273	B1	20011218	US 1995-473660	19950607
US 6352854	B1	20020305	US 1995-480147	19950607
US 6416714	B1	20020709	US 1995-484486	19950607
US 5874214	A	19990223	US 1995-538387	19951003
US 6025129	A	20000215	US 1995-567746	19951205
WO 9636436	A1	19961121	WO 1996-US6145	19960425
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 6100026	A	20000808	US 1996-633410	19960610
US 6319668	B1	20011120	US 1996-669252	19960624
US 6284459	B1	20010904	US 1996-711426	19960905
US 6017496	A	20000125	US 1996-709435	19960906
WO 9712680	A2	19970410	WO 1996-US15999	19961003
WO 9712680	A3	19970821		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9672573	A1	19970428	AU 1996-72573	19961003
EP 853497	A2	19980722	EP 1996-934064	19961003
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
WO 9749653	A2	19971231	WO 1997-US11035	19970624
WO 9749653	A3	19980226		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,				

GN, ML, MR, NE, SN, TD, TG

AU 9735779	A1	19980114	AU 1997-35779	19970624
US 6329139	B1	20011211	US 1997-912998	19970811
US 6340588	B1	20020122	US 1998-51022	19980922

PRIORITY APPLN. INFO.:

US 1995-428662	A2	19950425
US 1995-473660	A2	19950607
US 1995-480147	A2	19950607
US 1995-480196	A2	19950607
US 1995-484486	A2	19950607
US 1995-484504	A2	19950607
US 1995-538387	A2	19951003
US 1995-567746	A2	19951205
US 1996-639813	A2	19960402
WO 1996-US6145	A2	19960425
US 1996-633410	A2	19960610
US 1996-669252	A2	19960624
US 1996-711426	A2	19960905
US 1996-709435	A2	19960906
US 1995-184504	A2	19950607
US 1996-20706P	P	19960624
US 1996-723423	A	19960930
WO 1996-US15999	W	19961003
US 1996-726703	B2	19961007
US 1996-743984	A2	19961028
US 1996-741685	B2	19961031
US 1997-857800	B2	19970122
US 1997-826253	B2	19970327
WO 1997-US11035	W	19970624
US 1997-945053	B2	19971021

AB Combinations, called matrixes with memories, of matrix materials that are encoded with an optically readable code are provided. The matrix materials are those that are used as supports in solid phase chem. and biochem. syntheses, immunoassays and hybridization reactions. The matrix materials may addnl. include fluophors or other luminescent moieties to produce luminescing matrixes with memories. The memories include electronic and optical storage media and also include optical memories, such as bar codes and other machine-readable codes. By virtue of this combination, mols. and biol. particles, such as phage and viral particles and cells, that are in proximity or in phys. contact with the matrix combination can be labeled by programming the memory with identifying information and can be identified by retrieving the stored information. Combinations of matrix materials, memories, and linked mols. and biol. materials are also provided. The combinations have a multiplicity of applications, including combinatorial chem., isolation and purifn. of target macromols., capture and detection of macromols. for anal. purposes, selective removal of contaminants, enzymic catalysis, cell sorting, drug delivery, chem. modification and other uses. Methods for tagging mols., biol. particles and matrix support materials, immunoassays, receptor binding assays, scintillation proximity assays, non-radioactive proximity assays, and other methods are also provided. Ninety-six matrixes with memories were used to construct a 24-member peptide library by std. Fmoc peptide synthesis. An antibody generated to one of the peptides was used to study trends in binding to other members of the library.

REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L165 ANSWER 24 OF 53 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:759081 CAPLUS
DOCUMENT NUMBER: 126:16501
TITLE: Photoactivatable polymers for producing patterned biomolecular assemblies
INVENTOR(S): Conrad, David W.; Charles, Paul T., Jr.

Searched by Barb O'Bryen, STIC 308-4291

PATENT ASSIGNEE(S): Government of the United States of America, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633971	A1	19961031	WO 1996-US1496	19960201
W: CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5736257	A	19980407	US 1995-428454	19950425
US 5847019	A	19981208	US 1997-813144	19970307

PRIORITY APPLN. INFO.: US 1995-428454 19950425

AB The presently claimed invention is directed to novel **biochips** and a method for forming said **biochips** and novel photoactivatable compds. such as bis(((2,6-dinitrobenzyl)oxy)carbonyl)allyl **amine** (2,6-DOCA), bis(((2-nitrobenzyl)oxy)carbonyl)allyl **amine** (2-NOCA), and LC-ASA allyl **amine**. The invention relates to the prodn. of patterned biomol. assemblies, and esp. patterned network polymers formed upon substrates (e.g., silicon, glass), the network polymers capable of binding biomols. and biopolymers, e.g., nucleic acids, antibodies, proteins. The devices may be used in, e.g., immunoassays for **multiple** analytes by using **multiple** immobilized antibodies.

L165 ANSWER 25 OF 53 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2002:34734143 BIOTECHNO
TITLE: **Amine**-modified random **primers** to label probes for **DNA microarrays**
AUTHOR: Xiang C.C.; Kozhich O.A.; Chen M.; Inman J.M.; Phan Q.N.; Chen Y.; Brownstein M.J.
CORPORATE SOURCE: M.J. Brownstein, Laboratory of Genetics, National Institute of Mental Health, Natl. Human Genome Res. Institute, Bethesda, MD 20892, United States.
E-mail: mike@codon.nih.gov
SOURCE: Nature Biotechnology, (2002), 20/7 (738-742), 17 reference(s)
CODEN: NABIF0 ISSN: 1087-0156
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **DNA microarrays** have been used to study the expression of thousands of genes at the same time in a variety of cells and tissues. The methods most commonly used to label probes for **microarray** studies require a minimum of 20 .mu.g of total **RNA** or 2 .mu.g of poly(A) **RNA**. This has made it difficult to study small and rare tissue samples. **RNA** amplification techniques and improved labeling methods have recently been described. These new procedures and reagents allow the use of less input **RNA**, but they are relatively time-consuming and expensive. Here we introduce a technique for preparing fluorescent probes that can be used to label as little as 1 .mu.g of total **RNA**. The method is based on priming cDNA synthesis with random hexamer **oligonucleotides**, on the 5' ends of which are bases with free amino groups. These **amine**-modified primers are incorporated into the cDNA along with aminoallyl **nucleotides**, and fluorescent dyes are then chemically added to the free **amines**. The method is simple to execute, and **amine**-reactive dyes are considerably less expensive than dye-labeled bases or dendrimers.

L165 ANSWER 26 OF 53 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:34065426 BIOTECHNO
TITLE: **Attachment** of **benzaldehyde** -modified oligodeoxynucleotide probes to semicarbazide-coated glass
AUTHOR: Podyminogin M.A.; Lukhtanov E.A.; Reed M.W.
CORPORATE SOURCE: M.W. Reed, Epoch Biosciences, 21720 23rd Drive SE 150, Bothell, WA 98021, United States.
E-mail: mreed@epochbio.com
SOURCE: Nucleic Acids Research, (24 DEC 2001), 29/24 (5090-5098), 27 reference(s)
CODEN: NARHAD ISSN: 0305-1048
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Attachment of oligodeoxynucleotides (ODNs) containing **benzaldehyde** (BAL) groups to semi-carbazide-coated glass (SC-glass) slides is described. 5'-BAL-ODNs are prepared using automated **DNA** synthesis and an acetal-protected BAL phosphoramidite reagent. The hydrophobic protecting group simplifies purification of BAL-ODNs by reverse phase HPLC and is easily removed using standard acid treatment. The electrophilic BAL-ODNs are stable in solution, but react specifically with semicarbazide groups to give semicarbazone bonds. Glass slides were treated with a semicarbazide silane to give SC-glass. BAL-ODNs are coupled to the SC-glass surface by a simple one-step procedure that allows rapid, efficient and stable attachment. Hand-spotted arrays of BAL-ODNs were prepared to evaluate loading density and hybridization properties of immobilized probes. Hybridization to radiolabeled target strands shows that at least 30% of the coupled ODNs were available for hybridization at maximum immobilization density. The array was used to probe single **nucleotide** polymorphisms in synthetic **DNA** targets, and PCR products were correctly genotyped using the same macroarray. Application of this chemistry to manufacturing of **DNA microarrays** for sequence analysis is discussed.

L165 ANSWER 27 OF 53 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32158562 BIOTECHNO
TITLE: **Fabrication** of **DNA microarrays** using unmodified **oligonucleotide** probes
AUTHOR: Call D.R.; Chandler D.P.; Brockman F.
CORPORATE SOURCE: Dr. D.R. Call, Dept. of Vet. Microbiology/Pathology, Washington State University, P.O. Box 647040, Pullman, WA 99164-7040, United States.
E-mail: drcall@vetmed.wsu.edu
SOURCE: BioTechniques, (2001), 30/2 (368-379), 20 reference(s)
CODEN: BTNQDO ISSN: 0736-6205
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Microarrays** printed on glass slides are often constructed by covalently linking **oligonucleotide** probes to a derivatized surface. These procedures typically require relatively expensive **amine**- or thiol-modified **oligonucleotide** probes that add considerable expense to larger arrays. We describe a system by which unmodified **oligonucleotide** probes are bound to either nonderivatized or epoxy-silane-derivatized glass slides. Biotinylated PCR products are heat denatured, hybridized to the arrays, and detected using an enzymatic amplification system. Unmodified probes appear to detach

from the slide surface at high pH (> 10.0), suggesting that hydrogen bonding plays a significant role in probe attachment. Regardless of surface preparation, high temperature (up to 65.degree.C) and low ionic strength (deionized water) do not disturb probe attachment; hence, the fabrication method described here is suitable for a wide range of hybridization stringencies and conditions. We illustrate kinetics of room temperature hybridizations for probes attached to nonderivatized slides, and we demonstrate that unmodified probes produce hybridization signals equal to aminemodified, covalently bound probes. Our method provides a cost-effective alternative to conventional attachment strategies that is particularly suitable for genotyping PCR products with **nucleic acid microarrays**.

L165 ANSWER 28 OF 53 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1998:28247047 BIOTECHNO
TITLE: Immobilization of **DNA** in polyacrylamide gel for the **manufacture** of **DNA** and **DNA-oligonucleotide microchips**
AUTHOR: Proudnikov D.; Timofeev E.; Mirzabekov A.
CORPORATE SOURCE: A. Mirzabekov, Ctr. for Mech. Biology/Biotechnology, Argonne National Laboratory, 9700 South Cass Avenue, Argonne, IL 60439, United States.
E-mail: amir@everest.bim.anl.gov
SOURCE: Analytical Biochemistry, (15 MAY 1998), 259/1 (34-41), 26 reference(s)
CODEN: ANBCA2 ISSN: 0003-2697
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Activated **DNA** was immobilized in aldehyde-containing polyacrylamide gel for use in manufacturing the MAGIChip (**microarrays** of gel-immobilized compounds on a chip). First, abasic sites were generated in **DNA** by partial acidic depurination. Amino groups were then introduced into the abasic sites by reaction with ethylenediamine and reduction of the aldimine bonds formed. It was found that **DNA** could be fragmented at the site of amino group incorporation or preserved mostly unfragmented. In similar reactions, both amino-**DNA** and amino-**oligonucleotides** were attached through their **amines** to polyacrylamide gel derivatized with aldehyde groups. Single- and double- stranded **DNA** of 40 to 972 **nucleotides** or base pairs were immobilized on the gel pads to manufacture a **DNA microchip**. The **microchip** was hybridized with fluorescently labeled **DNA**-specific **oligonucleotide** probes. This procedure for immobilization of amino compounds was used to manufacture MAGIChips containing both **DNA** and **oligonucleotides**.

L165 ANSWER 29 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:488256 BIOSIS
DOCUMENT NUMBER: PREV200200488256
TITLE: **Oligonucleotide microarrays**: direct covalent attachment to glass.
AUTHOR(S): Beattie, Kenneth Loren (1)
CORPORATE SOURCE: (1) The Woodlands, TX USA
ASSIGNEE: Beattie; Kenneth L., Crossville, TN, USA
PATENT INFORMATION: US 6426183 July 30, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (July 30, 2002) Vol. 1260, No. 5, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.

ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention provides an improved method for stably attaching a desired compound to a silaceous or silane-containing substrate, in particular a glass, porous silica, or oxidized silicon. This method in certain embodiments provides improvements over conventional methods for attaching desired compounds to silaceous or silane-containing substrate, e.g., glass, porous silica, or oxidized silicon materials, e.g. obviating the need for derivatization (e.g., epoxysilane derivatization) prior to attachment. More particularly, the present invention provides a method for stably attaching a desired compound comprising at least one **amine** and hydroxyl group (e.g., an aminopropanol containing compound), to a silaceous or silane-containing substrate, preferably underivatized (plain) glass, a porous silica, or oxidized silicon substance. The subject method is especially useful for the attachment of **nucleic acid** sequences, e.g., **oligonucleotide** or PCR generated DNA fragments, to glass or other silane-containing substrates to which is stably attached to a desired compound, is useful in any application wherein a compound immobilized to a substrate, e.g., a glass, is useful. Such applications include, by way of example, hybridization analysis, DNA purification, immunoassay, and immunopurification methods.

L165 ANSWER 30 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:463726 BIOSIS
DOCUMENT NUMBER: PREV200200463726
TITLE: Developing site-specific immobilization strategies of **peptides** in a **microarray**.
AUTHOR(S): Lesaicherre, Marie-Laure; Uttamchandani, Mahesh; Chen, Grace Y. J.; Yao, Shao Q. (1)
CORPORATE SOURCE: (1) Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore, 117543: chmyaosq@nus.edu.sg Singapore
SOURCE: Bioorganic & Medicinal Chemistry Letters, (19 August, 2002) Vol. 12, No. 16, pp. 2079-2083. http://www.elsevier.nl/inca/publications/store/9/7/2/. print.
ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In **peptide**-based **microarrays**, most existing methods do not allow for site-specific immobilization of **peptides** on the glass surface. We have developed two new approaches for site-specific immobilization of kinase substrates onto glass slides: (1) slides were functionalized with avidin for attachment of biotinylated **peptides** ; and (2) slides were functionalized with thioester for attachment of N-terminally cysteine-containing **peptides** via a native chemical ligation reaction.

L165 ANSWER 31 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:552339 BIOSIS
DOCUMENT NUMBER: PREV200200552339
TITLE: Fabrication of **peptide microarrays** utilizing small-molecule affinity technology.
AUTHOR(S): Booth, Lisa R. (1); Clary, Scott T. (1); Gall, Anna S. (1); Hughes, Karin A. (1); Kaiser, Robert J. (1); Lund, Kevin P. (1); Spicer, Douglas A. (1)
CORPORATE SOURCE: (1) Prolinx, Inc., 22322 20th Ave. SE, Bothell, WA, 98021 USA
SOURCE: American Biotechnology Laboratory, (September, 2002) Vol. 20, No. 10, pp. 76, 78. print.
ISSN: 0749-3223.
DOCUMENT TYPE: Article

LANGUAGE: English

L165 ANSWER 32 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:540295 BIOSIS
DOCUMENT NUMBER: PREV200000540295
TITLE: Covalent attachment of **oligodeoxyribonucleotides** to **amine**-modified Si (001) surfaces.
AUTHOR(S): Strother, Todd; Hamers, Robert J.; Smith, Lloyd M. (1)
CORPORATE SOURCE: (1) Department of Chemistry, University of Wisconsin, 1101 University Avenue, Madison, WI, 53706-1396 USA
SOURCE: Nucleic Acids Research, (September, 2000) Vol. 28, No. 18, pp. 3535-3541. print.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A recently described reaction for the UV-mediated attachment of alkenes to silicon surfaces is utilized as the basis for the preparation of functionalized silicon surfaces. UV light mediates the reaction of t-butyloxycarbonyl (t-BOC) protected omega-unsaturated aminoalkane (10-aminodec-1-ene) with hydrogen-terminated silicon (001). Removal of the t-BOC protecting group yields an aminodecane-modified silicon surface. The resultant amino groups can be coupled to thiol-modified **oligodeoxyribonucleotides** using a heterobifunctional crosslinker, permitting the preparation of DNA arrays. Two methods for controlling the surface density of oligodeoxyribo-**nucleotides** were explored: in the first, binary mixtures of 10-aminodec-1-ene and dodecene were utilized in the initial UV-mediated coupling reaction; a linear relationship was found between the mole fraction of aminodecene and the density of DNA hybridization sites. In the second, only a portion of the t-BOC protecting groups was removed from the surface by limiting the time allowed for the deprotection reaction. The **oligodeoxyribonucleotide**-modified surfaces were extremely stable and performed well in DNA hybridization assays. These surfaces provide an alternative to gold or glass for surface immobilization of **oligonucleotides** in DNA arrays as well as a route for the coupling of **nucleic acid** biomolecular recognition elements to semiconductor materials.

L165 ANSWER 33 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-13720 BIOTECHDS
TITLE: Immobilizing nucleic acids on a solid support by contacting a support having immobilized thiol group with nucleic acids; dsDNA immobilization on glass, plastic, ceramic or metal support matrix for DNA **microarray** construction
AUTHOR: PATTERSON B C; MIELEWCZYK S; MAURER A J
PATENT ASSIGNEE: MATRIX TECHNOLOGIES CORP
PATENT INFO: WO 2002027026 4 Apr 2002
APPLICATION INFO: WO 2000-US30196 28 Sep 2000
PRIORITY INFO: US 2000-236287 28 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-405055 [43]
AB DERWENT ABSTRACT: NOVELTY - Immobilizing (M1) nucleic acid (NA) on a solid support (SS) comprising, providing SS having an immobilized thiol group in it and contacting SS with NA to react and form a bond between NA and the thiol group and to immobilize NA on SS, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) producing (M2) a **microarray** having multiples of single stranded NAs by providing SS having multiples of immobilized thiol groups in it, contacting SS with multiples of double-stranded NAs on the **microarray** by reacting the thiol groups with double-stranded NAs to form a bond between them, and denaturing the double-stranded immobilized NAs to form single-stranded NAs to produce a

microarray; (2) a kit (K1) for immobilizing multiples of NA on SS comprising SS having multiples of immobilized latent thiol groups in it and instructions for activating the thiol groups to form bonds with NA; (3) isolating (M3) a target NA in a sample by providing SS having at least one NA immobilized via reacting and forming a bond with at least one immobilized thiol, where NA has a nucleotide sequence complementary to a target NAs and contacting the immobilized NA with the sample under conditions sufficient to allow hybridization of target NAs to the immobilized NA to isolate the target NA from the sample; and (4) a NA **microarray** (NAM) comprising a solid support (SS) having multiples of immobilized thiol group in it, which is reacted and bonded with multiples of NAs to immobilize NA to SS. BIOTECHNOLOGY - Preferred Method: In M1, NA is from an unmodified NA, modified NA or a NA analog. NA is an oligonucleotide, a polymerase chain reaction product, or double or single stranded NAs. M1 further comprises contacting SS with a reagent containing a latent thiol group to provide SS having immobilized latent thiol group in it, activating the latent thiol group, and contacting SS with NA, where the immobilized NA forms **microarray**. In M2, double stranded NAs are denatured prior to contact with SS, such that multiples of single-stranded NAs react to form a bond with immobilized thiol groups. Preferred Kit: K1 further comprises an activator component, a latent thiol containing component or a wash buffer, where the activator component is dithiothreitol, beta-mercaptoethanol, tris-carboxyethyl phosphine or combinations of it and latent thiol-containing component is N,N'-bis(acryloyl)cystamine or 4-((1-oxo-3-((2-((1-oxo-2-propenyl)-amino) ethyl) dithio) propyl) amino) butanoic acid. Preferred **Microarray** : Thiol groups are thio containing materials is from thiol silanes, thiol containing monomers and polymers, disulfide-containing silanes, polymers or combinations of it. Thiol groups are latent and they are activated to be capable of reacting and bonding with NA. NAM comprising SS is formed from glass, plastic, ceramic or metal where SS comprises two or more spatially distinct regions, each region immobilizing at least one NA. USE - M1 is useful for immobilizing a NA on SS; M2 is useful for producing a **microarray** having multiples of single stranded NAs; and M3 is useful for isolating a target NAs in a sample (claimed). EXAMPLE - Preparation of glass supports with disulfide-containing polymeric coating (N,N'-bis(acryloyl)cystamine) (BAC-coated slides) was done using glass microscope slides which were cleaned and coated with an acrylic saline. The solution containing 103 ml N,N'-dimethyl formamide (DMF), 3.5 g BAC, 3.5 ml polyethylene glycol (PEG) 400 monoethyl-ether monomethacrylate and 57 ml millipore water was prepared and filtered. 5.4 ml of 10% ammonium persulfate (APS) and 100 mul of N,N,N',N'-tetramethylethylene diamine (TEMED) was added to above mentioned solution. The solution was mixed and poured into slide holder containing acrylic silanized slides. Polymerization of coating layer was allowed to proceed. After polymerization, the cloudy solution phase was decanted and slides were rinsed. Prior to probe spotting, slides were activated by soaking. Reduced slides were washed and dried. Activated slides were used, stored under ambient conditions without apparent loss of binding activity. Two **different oligonucleotide** probes were synthesized in 5'-Acrydite (RTM)-modified form, 5'-primary **amine** form, and unmodified form: 5'ATCTGCCCTCTTTGAAAAGCAAACTGAGGGCTCTGCTCGCTGGCCCTTCGGAGC CTACGAAGATCCAGCTGC-3' (ANF401-70) and 5'-CCAAAAATTATGGGGACATCATCGAAGCCCCT TGAGCATCTGACTTCTGGCT-3' (BG1236-50). Oligonucleotides were dissolved at 10 and 30 micromolar concentrations in 100 mM carbonate buffer pH 10, 0.01% sarkosyl, and spotted onto BAC- coated slides. Slides were hybridized with a mixture of 5.0 ng of Cy3-labeled rabbit reticulocyte cDNA spiked into 1.0mug of Cy3-labeled mouse cardiac cDNA and analyzed. In both cases, Acrydite (RTM)- modified probes gave higher hybridization signals than **amine**- modified or unmodified oligos. However, **amine**- modified and unmodified probes gave substantial hybridization signals, suggesting that at least two modes of probe binding to the support were occurring, only one of which was Acrydite

(RTM)-dependent.(41 pages)

L165 ANSWER 34 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-14258 BIOTECHDS
TITLE: Compound for binding macromolecule to substrate surface or conjugation targets, contains phosphorous containing reactive group, hydrazide protecting group and benzene ring, and has predefined formula;
DNA and **RNA** immobilization useful in **DNA chip** and **DNA** biosensor production
AUTHOR: RADDATZ S; MUELLER-IBELER J; SCHWEITZER M; BRUECHER C; WINDHAB N; HAVENS J R; ONOFREY T J; GREEF C H; WANG D
PATENT ASSIGNEE: NANOGEN INC
PATENT INFO: WO 2002014558 21 Feb 2002
APPLICATION INFO: WO 2000-US41663 11 Aug 2000
PRIORITY INFO: WO 2000-22205 11 Aug 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-404476 [43]
AB DERWENT ABSTRACT: NOVELTY - The compound for binding macromolecule to substrate surface or conjugation targets, is of formula (I). DETAILED DESCRIPTION - The compound for binding macromolecule to substrate surface or conjugation targets, is of formula (I): P1-O-La-Bz-(CONHNH-PGa)m. Bz = benzene ring; La = 1-12C hydrocarbon, with optional 1-4C ether or amide linkage; Pr = phosphorus bearing reactive group chosen from (a) and (b) Ra, Rb = 1-12C hydrocarbon; Rc = 2-cyanoethyl, allyl, methyl, ethyl and other alkyl moieties; Pga = hydrazide protecting group; and m = 1-3. INDEPENDENT CLAIMS are also included for the following: (1) compound of formula (II), (III), (IV), (V), or (VI); (2) method of producing modified macromolecule which involves contacting a macromolecule to be modified with a compound chosen from compound of formulae (I-VI), the macromolecule has a reactive hydroxyl group and phosphorus bearing reactive group, phosphorus forms a covalent bond with oxygen of reactive hydroxyl group, thus producing modified macromolecule; (3) modified macromolecule comprising compound (I) which is covalently attached to a macromolecule through Pr group; (4) Use of modified macromolecule in a conjugation reaction with a second molecule in solution, where the modified macromolecule is processed to produce at least one reactive hydrazide moiety on the modified macromolecule, the second molecule comprises a moiety reactive with hydrazide; and (5) substrate comprising immobilized macromolecules, where the immobilization linkage has structure (S). (II) is Pr-O-La-(CONHNH-PGa)m. m = 1-4 if m is greater than 1, La is branched. (III) is Pr-O-(CH2)n-Br-(-(CH2)p-Fl-Bz-(CONHNH-PGa)m)q Br = branching moiety chosen from carbon, nitrogen and benzene ring;Fl = **functional** linkage; n, p = 0-12; and q = 1-3. (IV) is Pr-O-(CH2)n-Bz-COORe. n = 1-12; and Re = 1-12C hydrocarbon (V) is Pr-O-(CH2)n-Br-(-(CH2)p-Fl-Bz-(COORe)m)q. (VI) is Pga = alcohol protecting group. S is Sub-(-RH-N(H)nNHOC-)m-L-PL-Ma. Sub = substrate material; Rh = linkage moiety comprising hydrazide-reactive center covalently attached to hydrazide; Lh = aliphatic or aromatic 1-50C hydrocarbon linker moiety, optionally with 1-10 hetero atoms chosen from oxygen, nitrogen, sulfur and phosphorus, in **functional** linkage; Pl = (c); Rp = hydrogen, electron pair, alkyl or cyano alkyl moiety; Ma = macromolecule; n = 0 if hydrazide is attached to Rh by double bond; and n = 1 if hydrazide is attached to Rh by single bond. USE - For binding macromolecules to substrate surface or other conjugation targets, such as in **DNA chip** technology, surface plasmon resonance experiments and biosensor applications. ADVANTAGE - Higher rate of immobilization, higher stability of attachment and potential to obtain higher amounts of immobilized oligosaccharide onto the substrate surface in less time, are enabled. Multiple binding sites per bound entity, stability in broad pH range, capability of molecular attachment under

anhydrous or aqueous conditions and molecular attachment to any solid phase surface are enabled. EXAMPLE - N-triphenylmethyl-6-hydroxycapronic hydrazide (in g) (3) in 50 ml of dry dichloromethane was slowly added to N-ethyldiisopropyl **amine** (4) and chloro(diisopropyl amino)-beta-cyanoethoxy phosphine (20.1) over 15 minutes. Upon complete addition, the reaction was stirred for 1 hour, concentrated, and chromatographed (ethyl acetate/n-heptane 2/3 with trace triethylamine) to obtain 6-((2cyanoethoxy)(diisopropyl amino) phosphanyloxy)-N'-tritylhexanohydrazide (3.19) as a pale yellow foam. Oligos (e.g. **DNA, RNA, peptide nucleic acid** (PNA), etc.) were synthesized using solid phase phosphoramidite chemistry on an automated oligo synthesizer. The phosphoramidite with the protected hydrazide was applied as 0.1 M solution in acetonitrile and coupled at the desired location in the sequence using standard activated reagents and coupling times. The CPG bound oligo (1 mmol) was placed in a 1.5 ml test tube and treated with 2.0 ml conc.NH4OH. After 2 hours, at 55 degreesC, the ammonia solution was removed and evaporated under reduced pressure. The trityl protected hydrazide oligo was purified by reverse phase high performance liquid chromatography (HPLC). The fractions containing the trityl-on product were pooled and evaporated and the trityl protecting group was removed by treating the oligo with 80 % acetic acid for 30 minutes at RT. The acid was removed in vacuo, and the residue was dissolved in water, then extracted twice with ethyl acetate. The aqueous layer was dried again and re-dissolved. Analytical HPLC showed a single product which was employed for further reactions without purification. Synthesis of oligo O9: Hydrazide-15 mer: (dp1a-TTTTTTTTTTTTTTT-3') involved synthesis and deprotection with amidite compound 1a. The trityl protected hydrazide oligo was purified by reverse phase HPLC using a Merck LiChrospher RP 18, 10 microM, column using 0.1 M triethylammonium acetate pH = 7.0 (TEAA) as buffer A and 75 % acetonitrile in buffer A as buffer B. A gradient of 0 % B to 100 % B in 100 minute was used for analytical and preparative separations. The trityl ON product eluted in 42.2 minutes.(120 pages)

L165 ANSWER 35 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-08811 BIOTECHDS
TITLE: Detecting nucleic acid (NA) variation comprises competitively hybridizing oligonucleotides to NA and extending them under gradually decreasing temperature conditions to differentiate matched and mismatched oligonucleotides;
DNA **microarray** for detecting lipoprotein gene mutation useful for diagnosis
AUTHOR: JANG G Y
PATENT ASSIGNEE: BIONEX INC
PATENT INFO: WO 2002004673 17 Jan 2002
APPLICATION INFO: WO 2000-KR753 12 Jul 2000
PRIORITY INFO: WO 2000-753 12 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-154939 [20]
AB DERWENT ABSTRACT: NOVELTY - Detecting sequence variation (SV) of nucleic acid (NA) comprising: (a) preparing a NA with possibility of having SV; (b) hybridizing to NA, 2 **different oligonucleotides** which have **different** detectable marker-labeled 5' end, and 3' end which has sequence complementary to 2 or more predetermined sequence variants of NA respectively; (c) extending NA at gradually decreasing temperature conditions; and (d) detecting extended NA products, is new. DETAILED DESCRIPTION - Detecting (M1) SV of NA, comprising: (a) preparing NA which has a possibility of carrying SV; (b) adding two or more **different oligonucleotides** which are complementary to the NA, and have 5' ends that are different detectable marker-labeled, and 3' end that is complementary to two or more different predetermined sequence variants of the NA respectively; (c) denaturing the NA by

heating; (d) hybridizing the oligonucleotides to the NA and extending using thermostable DNA polymerase under conditions of decreasing the temperature gradually; and (e) detecting a extended NA products. Optionally, the method comprises: (a) adding two or more **different** universal **oligonucleotides** which are not complementary to any sequence of the NA and 5' end of which are **different** detectable marker-labeled; (b) adding two or more **different oligonucleotides**, which consist of two parts of sequence, 5' side part of which have tail of the same sequence with the universal oligonucleotides, and 3' side part of which have sequence complementary to the different predetermined sequence variants of the NA, respectively; and (c) adding standard PCR oligonucleotides which are complementary to other strands of NA. BIOTECHNOLOGY - Preferred Method: The denaturation and hybridization steps are preferably repeated at least one time. The nucleic acid is prepared by polymerase chain reaction with two oligonucleotide primers which are normal unmodified oligonucleotide primers, 5' biotin-labeled oligonucleotide primers or 5' **amine** -labeled oligonucleotide primers. The prepared NA is preferably immobilized on glass plate, membrane and magnetic bead. Optionally, the nucleic acid is prepared by cutting cloned DNA using restriction enzyme. The oligonucleotides are uniform in their length and consist of 7-20 **nucleotides**. The 5' ends of the **oligonucleotides** are labeled with **different** fluorescent dyes. The **oligonucleotides** are hybridized to the **nucleic acid** and extended under a temperature condition which starts from 40-65 degrees C and is ramped down to 20-39 degrees C with cooling rate of 0.01-3 degrees C/second. Optionally, the temperature condition starts from 35-65 degrees C and is cooled down to 20-34 degrees C with a gradual step down of 0.1-4 degrees C. The NA hybridized to the **oligonucleotides** is extended by thermostable enzyme using four **different** nucleoside triphosphates, dATP, dGTP, dCTP and biotin-bound dUTP. The detection of extended products is achieved by using automated DNA sequencer, gel scanner or **Microarray** scanner. The method optionally involves: (a) preparing one or more nucleic acids which have a possibility of carrying several kinds of sequence variations; (b) adding several sets of two or more **different oligonucleotides** which are complementary to one or more **nucleic acid**, 5' end of which are **different** detectable marker-labeled and 3' end of which have sequence complementary to several kinds of two or more **different** predetermined sequence variants of the **nucleic acids** respectively; (c) denaturing the nucleic acids by heating; (d) hybridizing the oligonucleotides to the nucleic acid respectively and extending using thermostable DNA polymerase under the condition of decreasing the temperature gradually; and (e) detecting a extended nucleic acid products. The denaturation and hybridization steps are preferably repeated at least one time. USE - Detecting sequence variation of a nucleic acid (claimed). Analysis of sequence variation of nucleic acid is an important source of information for finding genes involved in biological process such as reproduction, development, aging and disease. Also, detecting sequence variation of DNA can be applied to the analysis of disease and diagnostic, therapeutic and preventative strategies. ADVANTAGE - The method is simple, cost effective, reliable and efficient. EXAMPLE - 32 samples of LIPC, a lipoprotein gene having fully defined sequence of 189 nucleotides (S1) as given in specification were obtained from thirty two peoples and amplified with two polymerase chain reaction (PCR) primers tctaggaagtggcagccag, acctttgtttgagggaagtgc. The amplified products were purified to remove excess of primers using conventional alcohol precipitation method. The sequence variation of T and C base appeared at 130th base of (S1) and two IRD700 and IRD800 dye-labeled oligonucleotides. Each purified DNA product was added in a reaction solution containing 10 mM Tris-HCl, pH 8.8, 2.9 mM MgCl2, 50 mM KCl and 200 mM of dNTP. Taq DNA polymerase, a 5' IR700 dye-labeled

oligonucleotide and 5' IR800 dye-labeled oligonucleotide were also added. This reaction solution was incubated at the ramping-down condition from 55 degrees C to 37 degrees C for 1 hour. After addition of stopping buffer containing 95% formamide and 0.1%. Bromophenol Blue, that was loaded to automated DNA Sequencer LI-COR 4200 and analyzed by electrophoresis. The result of electrophoresis showed that the signal or both IRD700 and IRD800 represented heterozygotic base T/C while the signal at only IRD700 and IRD800 represented homozygotic base T and C respectively. (28 pages)

L165 ANSWER 36 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-08424 BIOTECHDS
TITLE: Simultaneously genotyping multiple samples for characterizing diverse sources, comprises forming **microarrays** of genomic segments representing discrete loci and hybridizing with mixtures of synthetic oligonucleotides;
DNA **microarray** for use in cystic fibrosis, tyrosinemia, hereditary hearing loss, sickle cell anemia, galactosemia diagnosis
AUTHOR: SCHENA M A
PATENT ASSIGNEE: TELECHEM INT INC
PATENT INFO: WO 2002003849 17 Jan 2002
APPLICATION INFO: WO 2000-US21163 10 Jul 2000
PRIORITY INFO: US 2000-613006 10 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-148108 [19]
AB DERWENT ABSTRACT: NOVELTY - Simultaneously (M) genotyping multiple samples involves: (a) amplifying genomic segments comprising a distinct genetic locus from a number of samples using a number of primers; (b) forming a **microarray** on a surface from amplified segments; (c) hybridizing the **microarray** with a mixture of labeled synthetic oligonucleotides; and (d) deriving genotyping information by detecting signals from the hybridized **microarray**. DETAILED DESCRIPTION - Simultaneously (M) genotyping multiple segments involves: (a) amplifying a number of genomic segments from a number of samples using a number of polymerase chain reaction primers, each genomic segment comprising a distinct genetic locus; (b) forming a **microarray** on a surface from the amplified genomic segments, where each location on the surface contains amplified material derived from a single sample and consisting essentially of a single genomic segment; (c) hybridizing the **microarray** with a mixture of labeled synthetic oligonucleotides, where the mixture comprises oligonucleotides complementary to the genomic segments; and (d) deriving genotyping information simultaneously for the number of samples at the number of genetic loci by detecting signals from the hybridized **microarray**. BIOTECHNOLOGY - Preferred method: In (M), the number of samples comprises at least 10, preferably 5000 distinct samples. The genomic sequence comprise human disease loci. The samples are neonatal blood samples. The genetic loci comprise genetic loci associated with a human gene selected from beta-globin, cystic fibrosis transmembrane regulator protein (CFTR), and gut associated lymphoid tissue (GALT). The density of the **microarray** on the surface is at least 1000 spots/cm2. The **microarray** is formed by mechanical micro-spotting. The surface comprises glass and reactive aldehyde groups. The mixture of labeled synthetic **oligonucleotides** comprises ten **different** **oligonucleotide** sequences. The labeled synthetic **oligonucleotides** are between about 10 - 30 nucleotides in length, and comprises fluorescent labels (comprising dendrimer labels) or non-fluorescent labels. The genomic segments each comprise between about 40 - 1000 nucleotides. The amplified genomic segments comprise amino linkers. Hybridization is performed in an aqueous solution comprising salts and detergent, at a temperature about 10 degrees Centigrade below

the melting temperature of the labeled synthetic oligonucleotides. The genotyping information distinguishes samples from homozygotes and samples from heterozygotes at a specific genetic locus. The signals are generated by fluorescence emission from the labeled synthetic oligonucleotides, at more than one wavelength of light after antibody staining. USE - (M) is useful for simultaneously genotyping multiple samples (claimed). (M) is useful for characterizing samples from diverse biological sources, to screen for alleles from any plant or animal species, and for diagnosing diseases such as cystic fibrosis, tyrosinemia, maple syrup urine disease, alpha-1-antitrypsin deficiency, glutaric aciduria type I, hereditary hearing loss, beta-thalassemia, long chain 3-hydroxyl acyl CoA dehydrogenase deficiency, medium chain acyl CoA dehydrogenase deficiency, sickle cell anemia and galactosemia. ADVANTAGE - (M) enables broad screening of patients as well as other high-throughput application such as required for crop breeding in agriculture, forensics, and military application, as DNA isolation and polymerase chain reaction (PCR) processes are readily scaleable in either 96-well or 384-well configuration such that greater than 10000 samples per day are readily achieved in an automated laboratory setting. This throughput allows amplification of 10 loci from 240000 patients annually. EXAMPLE - Neonatal blood samples from 72 different newborns were isolated and amplified with gene-specific primers such as 5'-NAAACAGACACCATGGTGCAC-3', 5'-NCTGGCACCATTAAAGAAAAT-3', or 5'-NTGGGCTGTTCTAACCCCCAC-3'. These primer pairs contained reactive **amine** groups corresponding to the C6 amino modification, that allowed specific attachment of the amplicons to **microarray** substrate. The N position in each oligonucleotide sequence denoted the C6 amino modification. The primer pairs encompassed 5 discrete genomic segments corresponding to a total of three human genes: beta-globin, cystic fibrosis transmembrane regulator protein (CFTR), and gut associated lymphoid tissue (GALT). The diseases associated with the beta-globin, CFTR and GALT genes in human are sickle cell anemia, cystic fibrosis and galactosemia, respectively. The genomic segments encompassed five disease loci in the three genes and the approximate size of each amplicon was 60 base pairs. The genomic segments were amplified and then purified to remove contaminants. The purified products were re-suspended in 10 microliters of sterile, distilled water and 2 microliters of the 10 microliters was mixed with 2 microliters of 2X Micro-spotting solution, to provide a total of 4 microliters of sample for printing. The concentration for each polymerase chain reaction (PCR) amplicon in the sample plate was 100 micrograms/microliter. Each of the 72 samples of 4 microliters each were placed in adjacent wells of the 384-well plate, along with a total of 24 control samples containing either printing buffer alone or synthetic oligonucleotides. The 24 control samples provided both positive and negative hybridization controls in the experiments. A total of 96 samples (72 neonatal amplicons and 24 controls) were placed in a 384-well microplate so that all the wells in the first four rows each contained 4 microliters of sample. **Microarrays** of the 72 neonatal samples plus 24 control samples were formed into a **microarray**. All 96 samples were printed in triplicate (288 total spots) as 100 micrometer spots at 140 micrometer spot spacing such that each of the 4 pins produced a **microarray** subgrid containing 72 individual **microarray** spots. All 96 samples were then re-printed in triplicate at a 2 millimeter offset relative to the first **microarrays** to provide a duplicate set of spots for all 96 samples. The final **microarrays** each contained a total of 576 **microarray** spots in a total area of about 1.0 cm2. A total of 30 **microarrays** were printed on 30 SuperAldehyde **Microarray** Substrates, to allow for a variety of different hybridization mixtures and optimizations to be performed. Following the printing step, the **microarrays** were allowed to dry overnight at room temperature on the platten of the **microarraying** device and then processed to remove unbound DNA material, inactivate unreacted aldehyde groups and denature the printed PCR segments prior to

microarray hybridization. Hybridization mixtures were prepared using synthetic oligonucleotides complementary to an allele present in a specific amplicon. The alleles for the neonatal examples corresponded to disease loci of interest. To demonstrate direct detection, a mixture of 15-mers containing Cy3 or Cy5 labels was used. To demonstrate indirect detection, a mixture of 15-mers such as GACTCCTG(A/T)GGAGAA, TGGTGGTGAGGCCCT, ATCATCTTTGGTGTT, CACTGCCAGGTAAGG or CAACTGGAACCATTG containing biotin or dinitrophenol labels, was used. Hybridization reactions were performed using 10 microliters of the mixture per **microarray**. The 10 microliter mixture was applied to the **microarray** under a cover slip. Following hybridization, the **microarrays** were washed to remove unhybridized material, and the **microarrays** were detected for genotyping information. For the direct labeling experiments involving the mixture, the detection step was performed by scanning the **microarray** for fluorescence emission immediately following the wash step. Detection was performed using the ScanArray 3000 (RTM) confocal scanning instrument. The two-color capability of the scanner was used to detect fluorescent **microarray** signals in both the Cy3 and Cy5 channels corresponding to hybridization of the mixture of oligonucleotides. The data revealed that wild type, heterozygotes and homozygotes were readily distinguished in all of the examples examined from both the sickle cell and galactosemia loci. (26 pages)

L165 ANSWER 37 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-09845 BIOTECHDS
TITLE: New lollipop oligomer, useful for amplification and detection of nucleic acid, e.g. for mutational analysis, has two arms complementary to target and a tail, serving e.g. as primer; useful for diagnosis, SNP, DNA polymorphism, oncogene overexpression detection, expression profiling, gene discovery and mapping
AUTHOR: WARD D C; BRAY-WARD P; LANE M J; KUMAR G
PATENT ASSIGNEE: MOLECULAR STAGING INC; UNIV YALE
PATENT INFO: WO 2002002792 10 Jan 2002
APPLICATION INFO: WO 2000-US20933 30 Jun 2000
PRIORITY INFO: US 2000-215639 30 Jun 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-179634 [23]
AB DERWENT ABSTRACT: NOVELTY - Lollipop oligomer (I) is a branched oligomer with a tail part (T) and right and left arm parts (RA, LA) that are coupled together. Each arm has a target probe part, at its end, and a backbone part, and the probe parts are complementary to a target sequence (TS), having 5' and 3' regions. The LA and RA probe parts are complementary to the 3' and 5' regions of TS, respectively. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (A) amplifying nucleic acid (NA) using at least one (I); (B) detecting target NA using at least one (I); and (C) lollipop oligomers (Ia) similar to (I) and with T coupled at the junction of RA and LA. BIOTECHNOLOGY - Preferred Oligomers: In (I), T is (i) a rolling circle replication (RCR) primer that includes a part complementary to a primer-complementary portion of an amplification target circle (ATC); (ii) an address tag or (iii) complementary to at least part of the right and/or left backbone part. T and the two arms may form a triple helix and all are oligonucleotides (or the target portions are peptide nucleic acids). Particularly T and LA have free 3'-ends while RA has a free 5'-end. TS preferably includes a central part, between the 3'- and 5'-portions, and one of the probe regions in (I) is complementary to this part. Typically each arm contains 35-50 nucleotides (nt), with 20 nt in the probe parts; T is 10-35 nt, and ATC is 40-1000, preferably 50-100, nt. Preferred Process: In method (a), T includes an RCR primer and at least one each of (I) and target sample are incubated under hybridizing conditions. Before,

simultaneously with or after this step, at least one ATC is mixed with (I), followed by addition of a DNA polymerase so that replication of ATC occurs, forming a tandem-sequence DNA. Particularly at least one of the (I) used is a (Ia) and a ligase may be added, during or after the first step, so as to form locked (I), especially by ligation between the free ends of the arms. In this case, if TS includes a central region, then (i) one or more gap oligonucleotides, complementary to at least part of this central region, are also present and/or (ii) a gap-filling DNA polymerase is added, before or simultaneously with addition of ligase. Especially TS represents one form of a polymorphic sequence and then at least one probe portion is complementary to a polymorphic **nucleotide** in TS.
Particularly many **different** (I) are added, each complementary to different TS and used with RCR primers complementary to the same or different ATC. In method (b), T includes an address tag and this is used for detection of hybridization. USE - (I) are used for detection and/or amplification of nucleic acid sequences (claimed). Typical of very many applications are detection of many diseases, mutations, single nucleotide polymorphisms, viruses or overexpression of oncogenes; RNA expression profiling; gene discovery or mapping; assessing predisposition to diseases etc. ADVANTAGE - (I) provide specific and sensitive determination of the amount and location of nucleic acid sequences, and allow isothermal amplification (using T as rolling circle replication primer). Many different sequences can be detected simultaneously or in a single assay. EXAMPLE - Two oligonucleotides were synthesized, one for forming the right and left arm portions that hybridize to the target (padlock oligonucleotide), and the other as the tail portion that serves as the rolling circle replication primer (primer oligonucleotide). The allyl-amino side chain in the backbone of the first oligonucleotide was activated by reacting with Sulfo-GMBS and the primer (tail) oligonucleotide containing an SH group at its 5' end was generated by the treatment of S-S oligonucleotide with dithiothreitol (DTT). The arm portions with activated allyl-amino group and the tail oligonucleotide with the freshly generated SH group were reacted together to provide open lollipop oligomer that was purified by preparative poly-acrylamide gel electrophoresis (PAGE). 150microl aqueous solution of S-S primer oligonucleotide (7.5nmoles) was treated with 8 mg DTT and 5microl of triethyl **amine** for 30 minutes. The oligonucleotide with a free 5' SH group was purified by passing the reaction mixture through a PD-10 column. The purified oligonucleotide was freeze dried. 40microl of allyl amino oligonucleotide was mixed with 1mg N-(gamma-maleimidobutyrloxyl) sulfosuccinimide ester in 100 ml reaction buffer (50mM phosphate buffer, pH7.0, 150mM NaCl and 1mM EDTA) for 1 hour at 37degreesC. The activated allylamino oligonucleotide was purified on a PD-10 column and concentrated, the concentrated oligonucleotide was reacted with the freeze dried SH oligonucleotide for 1 hour at 37degreesC. The lollipop oligomer, the slowest migrating oligonucleotide band, was purified on an 8% PAGE gel. A typical (I) for detecting the wild-type G542X allele in the cystic fibrosis transmembrane conductance regulator gene consisted of right and left arms (3) and tail portion (4) 5'-pAAGAACTATATTGTCTTTCTGAGCGGATAACAAGA(allylamino-deoxyuridine)CACACAGGATACAGTATGACATGATTACGATGATTCCACCTTCTCC-3' (3) 5'-C6-S-S-C6-(A)25(C18)CGTCATCATGAACATTACACGTTCCAC (4). (4) is designed to function as primer for amplification of an amplification target circle (sequence reproduced). (53 pages)

L165 ANSWER 38 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-15535 BIOTECHDS
TITLE: Preparing biomolecular monolayer useful for preparing kits and biosensors for disease diagnosis, by reacting **functional** dendrimers on metal or glass surface with biomolecules e.g. **protein**, antigen, antibody, enzyme;
glucose-oxidase immobilization on solid support matrix for

biosensor and **protein** chip construction
AUTHOR: KIM H; YOON H; HONG M
PATENT ASSIGNEE: KIM H; YOON H; HONG M
PATENT INFO: US 2002006626 17 Jan 2002
APPLICATION INFO: US 2000-795604 15 Jul 2000
PRIORITY INFO: KR 2000-40829 15 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-328314 [36]
AB DERWENT ABSTRACT: NOVELTY - Preparing biomolecular monolayer, comprising reacting metal or glass surface with **amine**-terminated or succinimide-terminated alkanethiol for 1-2 hours to obtain self-assembled monolayer (I) that is reacted with **amine**-terminated, or N-hydroxysuccinimide-modified, carboxyl-terminated dendrimers (D) to give (D) monolayer (II), and reacting (II) with **protein**, antigen, antibody, enzyme receptor or **ligand**, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) preparing biomolecular monolayer based on strong interaction between avidin and biotin, comprising reacting (I) on metal or glass surface with **amine**-terminated (D) to obtain (II), reacting (II) with biotin to give biotinylated (II), and reacting biotinylated (II) with avidin to give avidin monolayer which is reacted with biotin-modified biomolecules; (2) preparing **microarray** of biomolecules by reacting metal surface or glass surface with a solution of alkane thiol or derivatized silane with **amine** reactive functionality to obtain (I), reacting (I) with **amine**-terminated (D) to give micropattern of (D), and reacting the patterned (D) with a biomolecule of **protein**, antigen, antibody, enzyme receptor or **ligand**; and (3) preparing **microarray** of biomolecules based on strong interaction between avidin and biotin which involves reacting micropattern of (D) with biotin to obtain biotin-modified **microarray** of (D), reacting the micropatterned, biotin-terminated (D) with avidin to give a **microarray** of avidin, and reacting the avidin **microarray** with the biotinylated biomolecule of **protein**, antigen, antibody, enzyme, receptor or **ligand**. BIOTECHNOLOGY - Preferred Method: In (M1), the metal or glass surface is reacted with an alkane thiol preferably cystamine dihydrochloride. (II) on a glass surface is obtained by reacting **amine** chain-end (D) on the surface of aldehyde silane-coated slide glass. (D) is any one of G1, G2, G3, G4 and G5 dendrimers containing **amine** groups, and G1.5, G2.5, G3.5, G4.5 and G5.5 dendrimers containing carboxyl groups modified with N-hydroxysuccinimide. Preferably, a monolayer of biomolecule containing **amine** groups or sugar chains is prepared by (M1), where the biomolecules containing **amine** groups are reacted with N-hydroxysuccinimide-modified, carboxyl-terminated (D), and biomolecules containing sugar chains are reacted with (D) containing **amine** groups after sugar chains are oxidized with periodate to have aldehyde groups. USE - Preparing biomolecular monolayers, where the biomolecule contains **amine** groups or sugar chains (claimed). The method is useful for preparing kits and biosensors for disease diagnosis and compound analysis using more recently, integrated high-throughput analyzing system such as development of **protein** chips. ADVANTAGE - Homogeneous high density monolayer of biomolecules can be prepared, and consideration of covalent bonding or orientation of **proteins** is not necessary. EXAMPLE - Preparation of monolayer using poly(amidoamine) dendrimers was carried out as follows. Silicon wafer with evaporated gold was cleaned with ethanol dipping and a self-assembled monolayer was obtained by immersing the washed base substrate in a solution of 5 mM dithiopropionic acid bis-N-hydroxysuccinimide ester in dimethylsulfoxide (DMSO) for 2 hours. After washing with methanol, the self-assembled monolayer thus obtained was immersed in a solution of 0.022 mM **amine**-terminated dendrimer in methanol for 1 hour to obtain a dendrimer monolayer. To prepare a

glucose oxidase monolayer, periodate-treated glucose oxidase solution was reacted with the dendrimer monolayer prepared above for 30 minutes to 1 hour. To stabilize imine linkage formed in this reaction, reduction was conducted using sodium borohydride compound for 30 minutes, and free aldehyde groups remained on their periphery of immobilized enzymes were blocked by treatment with 10 mM ethanolamine for 30 minutes. The characterization of glucose oxidase monolayer on the film prepared above was performed by electrochemical method as follows. The film with immobilized glucose oxidase was dipped into a buffer solution containing enzyme substrate and electron-transferring mediators, and then concentration of resulting immobilized enzyme was measured by registering resulting bioelectrocatalyzed current by applying voltage of 250 mV. The concentration of immobilized glucose oxidase was estimated by kinetic simulation as 1.7x10 to the power -12 mol/square cm. 80 % of immobilized enzyme activity was retained after 20 day storage in a buffer solution under room temperature.(9 pages)

L165 ANSWER 39 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-11417 BIOTECHDS
TITLE: Gene expression profile after intense second messenger activation in cortical primary neurones;
involving transcription factor, neurotrophic factor and neuropeptide expression profiling, **DNA chip** and real-time polymerase chain reaction
AUTHOR: MAYER P; AMMON S; BRAUN H; TISCHMEYER H; RIECHERT U; KAHL E; HOLLT V
CORPORATE SOURCE: Otto Von Guericke Univ
LOCATION: Hollt V, Otto Von Guericke Univ, Inst Pharmacol and Toxicol, Leipziger Str 44, D-39120Magdeburg, Germany
SOURCE: JOURNAL OF NEUROCHEMISTRY; (2002) 82, 5, 1077-1086
ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AUTHOR ABSTRACT - Numerous stimuli induce immediate early gene (IEG) expression in neurones,but a comprehensive overview of the late-response genes is lacking. Therefore we aimed to identify changes in the neuronal gene expression profile following intense stimulation. Forskolin and 12-O -tetradecanoylphorbol-13-acetate (TPA), direct activators of intracellular second messengers, were applied to primary cultured cortical neurones. The gene expression profiles were analyzed on Affymetrix **DNA chips** which cover around 8000 rat genes. Out of these, 95 genes (1.2%) were increased at least three-fold, and 43 genes (0.5%) were at least three-fold decreased. The gene chip results were verified by testing 15 of the altered genes by quantitative real-time PCR. The majority of the up-regulated genes were transcription factors, neurotrophic factors or (putative) neuropeptides. Furthermore, there were marked changesin intracellular signal processing enzymes and in postsynaptic structural **proteins** (e.g. vesl, arc, narp), which have been implicated in synaptic plasticity. Notably, classical players in neurotransmission or plasticity suchas glutamate and GABA receptors or voltage-gated ion channels were not increased. It is likely that the increased production of components of intracellular signalling and of postsynaptic **proteins** is involved in neuronal plasticity. (10 pages)

L165 ANSWER 40 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-04931 BIOTECHDS
TITLE: Immobilizing **polypeptides**, by contacting them to anchor molecules having nucleophile, so the ester/thioester groups of the **polypeptides** undergo trans-esterification to attach them to the anchor molecules on the surface;
involving vector-mediated gene transfer for expression in

host cell, for use in proteomics and high throughput screening

AUTHOR: NOCK S; SYDOR J
PATENT ASSIGNEE: ZYOMYX INC
PATENT INFO: WO 2001098458 27 Dec 2001
APPLICATION INFO: WO 2000-US19531 19 Jun 2000
PRIORITY INFO: US 2000-212620 19 Jun 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-114573 [15]

AB DERWENT ABSTRACT: NOVELTY - Immobilizing a **polypeptide** (I) comprising an ester or thioester (E/T) to a surface, by contacting (I) to an anchor molecule (II) comprising a nucleophilic group (N1) at 2 or 3 position relative to a second nucleophilic group, so the E/T undergoes a trans-esterification reaction with N1 to form an intermediate compound in which (I) is attached to (II) through N1, and attaching (II) to the surface. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an array (A1) of immobilized **polypeptides** attached to a surface (A1 comprises at least a first **polypeptide** species and a second **polypeptide** species and each of the **polypeptide** species are attached to a separate region of the surface in same orientation, and are folded in a secondary structure as required for a biological activity); (2) an array (A2) of immobilized **polypeptides** attached to a surface which comprises a number of surface regions (each surface region has attached to a **polypeptide** species and a **polynucleotide** that encodes the **polypeptide** species); (3) screening (M1) a library of **nucleic acids** to identify a **nucleic acids** that encodes a **polypeptide** having a desired activity, by expressing a number of fusion **proteins**, each of which is encoded by an expression cassette that comprises a member of the library of **nucleic acids**, an intein coding region, and an open reading frame that encodes a **polypeptide** that is displayed on a surface of a replicable genetic package (the fusion **proteins** are displayed on the surface of a replicable genetic package) and screening the replicable genetic packages to identify those that display a **polypeptide** having the desired activity; (4) a **nucleic acid** (III) that comprises an expression cassette, comprising an insertion site at which a **polynucleotide** can be introduced into the expression cassette, an intein coding region (the carboxy terminus of the intein coding region is mutated so that it does not function as a splice junction for intein-mediated cleavage), and an open reading frame that encodes a **polypeptide** that is displayed on a surface of a replicable genetic package (the introduction of a **polynucleotide** at the insertion site results in an open reading frame that encodes a fusion **protein** which comprises a **polypeptide** encoded by the **polynucleotide**) which **polypeptide** is attached at its carboxyl terminus to an amino terminus of the intein, and the surface-displayed **polypeptide** is attached to the carboxy terminus of the intein; and (5) a kit for use in immobilizing one or more **polypeptides** containing E/T to a surface of a substrate, comprising an anchor molecule reagent for adapting E/T containing **polypeptide** to the surface. WIDER DISCLOSURE - The following are also disclosed: (1) expression cassettes and expression vectors that facilitates the use of display on replicable genetic packages for initial screening, followed by intein-mediated derivatization of the **polypeptide**; (2) synthesizing arrays comprising (I); (3) biosensors, micromachined devices, and diagnostic devices that comprise the **polypeptide** arrays; and (4) transferring a target molecule to a reaction chamber, provides solution or condition that dissociates the target molecule from the affinity molecule. BIOTECHNOLOGY - Preferred Method: The intermediate compound undergoes an intramolecular rearrangement in which the second

nucleophilic group (N2) on (II) displaces N1, therefore forming a more stable bond between (II) and (I). In M1, the **polypeptide** encoded by the library member is released from the fusion **protein** by contacting the phage with a nucleophilic compound, which becomes attached to the **polypeptide**. The nucleophilic compound comprises a compound having N1 and N2. The nucleophilic compound is a 2-aminonucleophile or a 3-aminonucleophile or an aminothiol or a 3-aminothiol, and comprises a thiol or a hydroxyl. Preferred Molecule: (I) comprises a thioester. (II) comprises a 2-aminonucleophile e.g. 2-aminothiol or 3-aminonucleophile. (II) comprises a structure (S1) or (S2), and is attached to the surface prior to or after contacting (I). (II) comprises a functional group that can be covalently linked to a molecule that is attached to the surface, where the function group is selected from ketone, diketone, **olefin**, epoxide, aldehyde, reactive ester, isocyanate, thioisocyanate, carboxylic acid chloride, disulfide, sulfonate ester, maleimide, isomaleimide, N-hydroxysuccinimide, nitrilotriacetic acid, activated hydroxyl, haloacetyl, activated carboxyl, hydrazide, epoxy, aziridine, sulfonylchloride, acyl hydrazine, trifluoromethyldiaziridine, pyridyldisulfide, N-acyl-imidazole, imidazolecarbamate, vinylsulfone, succinimidylcarbonate, arylazide, anhydride, diazoacetate, benzophenone, isothiocyanate, isocyanate, imidoester, aminooxy or fluorobenzene. (II) comprises a tag group that can be non-covalently bound to a molecule that is attached to the surface. The tag comprises a binding domain derived from glutathione-S-transferase (GST), streptavidin or green-fluorescent **protein** (GFP). The tag comprises a **peptide** that comprises an amino-terminal Cys, Thr or Ser. (I) comprises a non-natural amino acid, and E/T is chemically introduced onto (I) by chemical synthesis of the **polypeptide**. (I) is obtained by expressing a chimeric gene that encodes a fusion **protein** and contacting the fusion **protein** with a nucleophilic compound which releases the **polypeptide** from the intein at the splice junction and forms (I). The fusion **protein** comprises the **polypeptide** and an intein, or its functional portion, which is joined to the **polypeptide** at a splice junction at the amino terminus of the intein, where the carboxyl terminus of the intein lacks a functional splice junction. The nucleophilic compound is the anchor molecule and comprises a **peptide**. The **peptide** comprises a serine, threonine or cysteine at its amino terminus, the oxygen and sulfur of which are the nucleophilic groups that undergo the transesterification reaction. The nucleophilic compound comprises a thiol as the nucleophile. The intein is an Int-n of a split intein and (II) comprises an amino acid sequence that comprises an Int-c of a split intein, where the Int-n and Int-c undergo an intein splicing reaction, therefore attaching (II) to (I). Int-n is derived from a dnaE-n gene and the Int-c is derived from a dnaE-c gene. The dnaE-n gene and dnaE-c gene are from a cyanobacterium species e.g. Synechocystis sp.. The fusion **protein** is expressed in vitro or in vivo by introducing the chimeric gene into a host cell and incubating the host cell under conditions conducive to expression of the fusion **protein**. The surface on which (I) is immobilized, comprises a **biochip** comprising a non-sample surface and a number of sample portions that are elevated with respect to the non-sample surface, and each sample portion has attached to a single **polypeptide** species. The **biochip** comprises one or more materials selected from silicon, plastic, gold and glass. Alternately, the surface comprises a microparticle, and (I) is placed in contact with the surface using a microvolume dispenser that comprises a body and at least one vertical channel defined within the body, the channel being defined by at least one passive valve, where an interior surface defining at least one vertical channel is hydrophobic. The dispenser comprises a number of vertical channels defined within the body and arranged as an array. Each of the **peptide** species in A1, are covalently attached to the surface-bound linker by a 2-aminonucleophile ester bond

e.g. 2-aminothioester bond, which undergoes an intramolecular rearrangement to form an amide bond. The linker is a non-**peptide** linker and the C-terminus of each of the **polypeptide** is attached to the surface. The linker comprises the structure S1 or S2. The expression cassette of (III) further comprises a promoter. (III) is a member of a library of **polynucleotides** such as library of cDNA molecules, genomic **DNA** fragments or recombination products. (II) comprises a NH2-NH-R and an aminooxy group, where R represents (II), E/T reacts with the reactive group, therefore forming a compound comprising (I) attached to (II) through a reactive group. Preferred Kit: The kit further comprises a **DNA** vector for introducing E/T into the **polypeptide**, where the vector is adapted to receive a **nucleic acid** sequence encoding the **polypeptide** to form a E/T **polypeptide** expression vector for expressing the **polypeptide** as an E/T **polypeptide**. The kit further comprises a chemical agent for introducing E/T into (I), and instructions for instructing a user to carry out the immobilization method using the kit. The kit further comprises a substrate for attaching (II) immobilizing (I), where (II) is supplied attached to the surface of the substrate for later attaching (I) by a user. (I) is supplied with a kit precoupled with (II). USE - The methods are useful for immobilizing **polypeptides** and for forming arrays of **polypeptides** (claimed). The immobilized **polypeptides** are useful for proteomics and high-throughput screening. ADVANTAGE - The immobilized **polypeptides** are generally in the same orientation, are of full length and biologically active, and can be readily screened for a desired activity. EXAMPLE - None given.(61 pages)

L165 ANSWER 41 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-05756 BIOTECHDS
TITLE: Labeling RNA using a process of signal amplification where labeled agents are bound to the initial label increases the signal and reduces the ratio of signal to background, and is useful for detecting RNA or DNA in a sample;
labeled RNA probe, polymerase chain reaction, DNA primer, capture DNA probe and DNA array for Mycobacterium tuberculosis RNA or DNA detection
AUTHOR: LAAYOUN A; DO D; MIYADA C G
PATENT ASSIGNEE: LAAYOUN A; DO D; MIYADA C G
PATENT INFO: US 2001044105 22 Nov 2001
APPLICATION INFO: US 1999-737761 17 Dec 1999
PRIORITY INFO: US 2000-737761 18 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-121352 [16]
AB DERWENT ABSTRACT: NOVELTY - Labeling an RNA with signal amplification, comprising fragmenting the RNA, fixing a ligand to a terminal phosphate of the 3' and/or 5' ends of each fragment, and binding labeling agents to the ligands, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a labeled RNA fragment obtained by the process of the main claim, which comprises at the 3' or 5' end, a single nucleotide which is labeled at the terminal phosphate released during fragmentation; (2) a labeled RNA fragment comprising at the 3' end a phosphate or thiophosphate bearing a fluorescein bound to an anti-fluorescein antibody bearing at least one biotin, where the antibody is bound to a labeled streptavidin; (3) detecting an RNA or DNA comprising probing a sample with one of the above labeled RNA fragments; and (4) binding a labeled target to a capture probe, comprising exposing the target to the capture probe, where the target is one of the above labeled RNA fragments. BIOTECHNOLOGY - Preferred Method: Binding the label to the ligand is preferably indirect, with an anti-ligand being bound to the ligand, a second ligand being bound to the anti-ligand and a labeled second anti-ligand being bound to the second ligand. Preferably

the first ligand/anti-ligand and second ligand/anti-ligand combinations are either biotin/streptavidin, hapten/antibody, antigen/antibody, peptide/antibody, sugar/leptin or polynucleotide/complementary polynucleotide, most preferably where the first ligand is a biotin derivative and the label a streptavidin derivative. The first and second **ligands** may be the same or **different**, and where **different** the first **ligand** is preferably a fluorescein derivative and the second a biotin derivative. The fragmentation and fixing steps are effected in one or two steps. The binding of the labeling agent to the first ligand is covalent or non-covalent. Fixing is preferably effected by reacting a reactive function carried by the first ligand to a phosphate at position 2' or 3' or in the cyclic monophosphate 2'-3' position with respect to a ribose at the 3' of 5' end of the RNA fragment. The reactive function may be a nucleophilic, electrophilic or halide function. Alternatively an R-X molecule may be linked to that phosphate, where R = is the first ligand and X = is a hydroxyl, **amine**, hydrazine, alkoxylamine, alkyl halide, phenylmethyl halide, iodacetamide or maleimide. Specifically, R-X is 5-(bromofluoroscein) or a derivative of iodoacetyl biotin. Fragmenting may be effected enzymatically (preferably with a nuclease), physically (preferably by sonication or irradiation), or chemically (preferably with metal cations optionally combined with a chemical catalyst). The metal cations are selected from Mg2+, Mn2+, Cu2+, Co2+ or Zn2+ , optionally combined with a chemical catalyst, more preferably imidazole, a substituted imidazole analog, or any chemical molecule which carries an imidazole nucleus or a substituted imidazole analog. Preferred RNA Fragment: This is 10-150 nucleotides long. The fragment comprises at least one nucleotide having a thiophosphate group which is attached to a biotin bound to a streptavidin. USE - The invention is used in the detection of RNA or DNA in a sample. EXAMPLE - Total nucleic acids were isolated from Mycobacterium tuberculosis and the 16S hypervariable region was polymerase chain reaction (PCR) amplified using standard technique with primers containing a bacteriophage T3 or T7 promoter at the 5' end and having positions 213-236 and 394-415 of the M. tuberculosis reference sequence M209v0 (GenBank). Promoter tagged PCR amplicons were used for generating labeled single stranded RNA targets by in vitro transcription using T3 or T7 polymerase. To 1 microlitres RNA molecules was added 6 microlitres 0.1 M imidazole, 6 microlitres 1 M MnCl2, 2 microlitres 5-(bromomethyl)fluorescein (5-BMF; 100 mM in DMSO) and water to a final volume of 100 microlitres. Reaction medium was homogenized and incubated at 65 degrees Centigrade for 30 mins. Analysis was performed using a **DNA chip** as described in A. Troesch et al., J. clin. Microbiol., 37(1), pp49-55, 1999. After hybridization the arrays were washed and a second step of staining was performed using staining solution containing 300 microlitres 2 M MES, 2.4 microlitres acetylated bovine serum albumin (BSA), 6 microlitres normal goat IgG, 1.2 microlitres anti-fluorescein antibody and water to a final volume of 600 microlitres. The results in terms of nucleotide base call percentage, mean signal intensities for probe array cells(S) , mean background intensities (B) and S/B ratios were 91.4%, 9095 relative fluoresence unit (RFU), 4179 RFU and 2.2 respectively for direct labeling with 5-BMF, whilst the figures for antibody staining were 99.5%, 17884 RFU, 2049 RFU and 8.7 respectively. This data showed that the signal amplification using antibody staining improves base call percentage and intensity level. The ratio signal versus background is also improved.(5 pages)

L165 ANSWER 42 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-02202 BIOTECHDS
TITLE: Base material for **DNA chips** useful in gene analysis, comprises saturated hydrogenated ring-opened polymer of cyclic **olefin** or saturated hydrogenated copolymer of alpha-**olefin**, having preset heat

deflection temperature;
heat-resistant 5-methyl-2-norbornene support matrix for **DNA chip** manufacture and Rickettsia sp. infection diagnosis
PATENT ASSIGNEE: Sumitomo-Bakelite
LOCATION: Japan.
PATENT INFO: JP 2001231556 28 Aug 2001
APPLICATION INFO: JP 2000-43743 22 Feb 2000
PRIORITY INFO: JP 2000-43743 22 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2001-613790 [71]
AB A base material for **DNA chips** is new and contains a saturated cyclic **polyolefin** type polymer such as a saturated polymer which has been hydrogenated after ring-opening polymerization of a cylic **olefin** derivative or a saturated polymer hydrogenated to a copolymer of alpha-**olefin** or cyclic **olefin** derivative. The heat deflection temp. of the polymer is 95 deg or more. Also claimed is a **DNA chip** containing the base material. The base material is useful for manufacturing **DNA chips** for gene analysis of diseases caused by bacteria, especially Rickettsia sp. pathogens. The base material has excellent injection moldability, self-fluorescent property and heat-resistance. In an example, an open-ring polymer hydrogenated substance of 5-methyl-2-norbornene having heat deflection temp. of 123 deg, was injection molded with hydrogen at a rate of 21 g/10 min, at 280 deg and 130 MPa. The obtained injection molded product when evaluated showed excellent injection moldability, self-fluorescent property and heat-resistance.

L165 ANSWER 43 OF 53 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 1997-00038 BIOTECHDS
TITLE: Chemical methods of DNA and RNA fluorescent labeling; DNA depurination and RNA 3'-terminal ribonucleoside oxidation for hybridization with oligonucleotide microchip
AUTHOR: Proudnikov D; *Mirzabekov A
CORPORATE SOURCE: Argonne-Nat.Lab.; Engelhardt-Inst.Mol.Biol.Moscow
LOCATION: Center for Mechanistic Biology and Biotechnology, Argonne National Laboratory, 9700 South Cass Avenue, Argonne, IL 60439, USA.
Email: amir@everest.bim.anl.gov
SOURCE: Nucleic Acids Res.; (1996) 24, 22, 4535-42
CODEN: NARHAD
ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several procedures have been described for DNA and RNA fluorescent labeling, based on sodium periodate-mediated introduction of aldehyde groups by partial DNA depurination or 3'-terminal ribonucleoside oxidation in RNA. Fluorescent labels with an attached hydrazine group are coupled with the aldehyde groups and the hydrazone bonds are stabilized by reduction with sodium cyanoborohydride. DNA can also be split at the depurinated sites with ethylenediamine. The aldimine bond between the aldehyde group in depurinated DNA or oxidized RNA and ethylenediamine is stabilized by reduction with sodium cyanoborohydride and the primary **amine** group introduced at these sites is used for attachment of isothiocyanate of succinimide derivatives of fluorescent dyes. Fluorescent DNA labeling can be carried out in solution or on a reverse-phase column. These procedures provide simple, inexpensive methods of **multiple DNA** labeling and of introducing one fluorescent dye molecule per **RNA**, as well as quantitative DNA fragmentation and incorporation of one label per fragment, for labeled RNA, DNA and DNA fragment hybridization with

oligonucleotide microchips. (42 ref)

L165 ANSWER 44 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-454510 [48] WPIDS
DOC. NO. CPI: C2002-129205
TITLE: Sequencing nucleic acids by detecting the identity of a nucleotide analogue (I) after its incorporation into the growing strand of DNA by using 4 (I) each labeled with unique label, and self-priming the immobilized DNA template.
DERWENT CLASS: B04 D16
INVENTOR(S): EDWARDS, J R; ITAGAKI, Y; JU, J; LI, Z
PATENT ASSIGNEE(S): (EDWA-I) EDWARDS J R; (ITAG-I) ITAGAKI Y; (JUJJ-I) JU J; (LIZZ-I) LI Z; (UYCO) UNIV COLUMBIA NEW YORK
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002029003	A2	20020411	(200248)*	EN	121
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 2002102586	A1	20020801	(200253)		
AU 2001096645	A	20020415	(200254)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002029003	A2	WO 2001-US31243	20011005
US 2002102586	A1 CIP of Provisional	US 2000-684670	20001006
		US 2001-300894P	20010626
		US 2001-972364	20011005
AU 2001096645	A	AU 2001-96645	20011005

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001096645	A Based on	WO 200229003

PRIORITY APPLN. INFO: US 2001-300894P 20010626; US 2000-684670 20001006; US 2001-972364 20011005

AB WO 200229003 A UPAB: 20020730
NOVELTY - Sequencing (M1) a nucleic acid (NA) by detecting the identity of a nucleotide analogue (I) after (I) is incorporated into a growing strand of DNA in a polymerase reaction involves use of 4 (I) each labeled with a unique label, and a cleavable chemical group capping the 3'-position of deoxyribose and an immobilized DNA template that is able to self-prime for initiating the polymerase reaction.

DETAILED DESCRIPTION - Sequencing a NA by detecting the identity of (I) after (I) is incorporated into a growing strand of DNA in a polymerase reaction, comprises:

(i) attaching a 5' end of NA to a solid surface;

(ii) attaching a primer to NA attached to the solid surface;

(iii) adding polymerase and 1 or more different (I) to NA to incorporate (I) into the growing strand of DNA (the incorporated (I) terminates the polymerase reaction, and each different (I) comprises:

(a) a base such as adenine, guanine, cytosine, thymine, uracil (or

analogues);

(b) a unique label attached through cleavable linker to the base or to an analogue of the base;

(c) a deoxyribose; and

(d) a cleavable chemical group to cap an -OH group at a 3'-position of the deoxy ribose;

(iv) washing the solid surface to remove unincorporated (I);

(v) detecting the unique label attached to (I) that has been incorporated into the growing strand of DNA (so as to therefore identify the incorporated (I));

(vi) adding one or more chemical compounds to permanently cap any unreacted -OH group on the primer attached to NA or on a primer extension strand formed by adding one or more nucleotides or (I) to the primer;

(vii) cleaving the cleavable linker between the (I) that was incorporated into the growing strand of DNA and the unique label;

(viii) cleaving the cleavable chemical group capping the -OH group at -the 3'-position of the deoxyribose to uncap the -OH group, and washing the solid surface to remove cleaved compounds; and

(ix) repeating steps (iii)-(viii) to detect the identity of a newly incorporated NA into the growing strand of DNA (if the unique label is a dye, the order of steps (v)-(vii) is: (v), (vi) and (vii), and if the unique label is a mass tag, the order of steps (v)-(vii) is: (vi), (vii), and (v)).

INDEPENDENT CLAIMS are also included for the following:

(1) attaching (M2) a NA to a solid surface by coating the solid surface with a phosphine group, attaching an azido group to the 5' end of NA and immobilizing the 5' end of NA to the solid surface through interaction between the phosphine group on the solid surface and the azido group on the 5' end of NA;

(2) a nucleotide analogue which comprises a base such as adenine, cytosine, guanine, thymine or uracil (or analogues), a unique label attached through a cleavable linker to the base (or to an analogue), a deoxyribose, and a cleavable chemical group to cap an -OH group at a 3'-position of the deoxyribose; and

(3) a parallel mass spectrometry system (II), which comprises several atmospheric pressure chemical ionization mass spectrometers for parallel analysis of several sample comprising mass tags.

USE - (M1) Is useful for simultaneously sequencing several different NAs. (M1), (I) Or (II) are also useful for detection of single nucleotide polymorphism, genetic mutation analysis, serial analysis of gene expression, gene expression analysis, identification in forensics, genetic disease association studies, DNA sequencing, genomic sequencing , translational analysis, or transcriptional analysis. (M2) is useful for gene expression analysis, **microarray**

based gene expression analysis, mutation detection, translational analysis, or transcriptional analysis (claimed).

ADVANTAGE - The method allows development of ultrahigh-throughput and high-fidelity DNA sequencing system for polymorphism for phamacogenetics applications and for whole genome sequencing.

Dwg.0/24

L165 ANSWER 45 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-217233 [27] WPIDS
DOC. NO. NON-CPI: N2002-166432
DOC. NO. CPI: C2002-066524
TITLE: Protein **microarray** for screening complex chemical or biological samples to identify, isolate, and/or quantify components within complex samples, includes solid support, linker and protein or protein fragment.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): CARDONE, M H; MACBEATH, G; MARKS, J D; NIELSEN, U; SINSKY, A; SORGER, P

PATENT ASSIGNEE(S): (MASI) MASSACHUSETTS INST TECHNOLOGY; (CARD-I) CARDONE M H; (MACB-I) MACBEATH G; (MARK-I) MARKS J D; (NIEL-I) NIELSEN U; (SINS-I) SINSKY A; (SORG-I) SORGER P

COUNTRY COUNT: 96

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002012893	A2	20020214	(200227)*	EN	49

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001077245 A 20020218 (200244)

US 2002076727 A1 20020620 (200244)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002012893	A2	WO 2001-US24264	20010803
AU 2001077245	A	AU 2001-77245	20010803
US 2002076727	A1 Provisional	US 2000-222763P	20000803
		US 2001-921655	20010803

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001077245	A Based on	WO 200212893

PRIORITY APPLN. INFO: US 2000-222763P 20000803; US 2001-921655 20010803

AB WO 200212893 A UPAB: 20020429

NOVELTY - A protein **microarray** (I) comprising a solid support (10), a linker (20) and a protein or protein fragment, is new. The linker is covalently attached to the solid support, and the protein or protein fragment has a terminus that is capable of forming a covalent bond with the linker.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) attachment of a protein to a support surface, comprising:

(a) covalently attaching a bovine serum albumin (BSA) to a solid support surface;

(b) forming an activated carbamate group or activated ester group on the exposed surface of the molecule; and

(c) exposing the activated carbamate or ester group to a binding element comprising an **amine** to form a covalent bond between the carbamate or ester group of the molecule and the **amine** group of the binding element.

(2) attachment of protein to a support surface (M2), comprising:

(a) providing a support surface comprising a first chemical group available for reaction;

(b) providing a capture protein comprising a first terminus and a second terminus, where the first terminus is capable of binding to the ligand and the second terminus comprises a second chemical group; and

(c) forming a covalent bond between the first and second chemical groups, thus attaching the capture protein to the support surface at the second terminus of the capture protein;

(3) identification of small molecule that regulates protein binding (M3) comprising:

(a) attaching a capture protein (30) on support surface, exposing the substrate surface to a ligand for the capture protein and small molecule(s);

(b) and detecting the presence or absence of binding between the capture protein and the ligand;

(4) identification of a small molecule that selectively affects a cellular pathway (M4), comprising:

(a) attaching a **microarray** of capture proteins on a support surface comprising proteins that act in a cellular pathway;

(b) exposing the substrate surface to at least one ligand of the capture proteins and at least one small molecule;

(c) detecting a change in binding, which results from interaction with the small molecule, between the capture proteins and ligand;

(5) labeling an antigen (M5) comprising digesting the antigen with a protease to produce **multiple peptides**, so that at least one of the peptides is capable of receiving a label at a region of the peptide that does not interfere with binding between an epitope on the peptide and an antibody or antibody fragment;

(6) detection of phosphorylated protein (M6) comprising:

(a) fragmenting a candidate protein into peptides comprising target peptide with phosphorylation site;

(b) exposing the peptides to an antibody or antibody fragment having affinity for an epitope on the target peptide;

(c) selecting the target peptide based on affinity of the target peptide for antibody or antibody fragment; and

(d) conducting mass spectrometry on the target peptide; and

(7) studying a cellular event (M7) comprising:

(a) attaching a capture molecule on a support surface;

(b) exposing the substrate surface to a solution containing cellular organelle; and

(c) capturing the organelle through binding between the capture molecule and the ligand.

USE - The **microarray** is useful for screening complex chemical or biological samples to identify, isolate and/or quantify components within a sample based on their ability to bind to specific or wide variety of binding elements.

ADVANTAGE - The inventive **microarray** enables high-throughput screening of very large numbers of compounds. It paves the way for extensive and efficient screening using antibodies and similar molecules.

DESCRIPTION OF DRAWING(S) - The figure shows proximal phospho-affinity mapping.

Solid support 10

Linker 20

Capture protein 30

Dwg.2/11

L165 ANSWER 46 OF 53 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-424925 [45] WPIDS

DOC. NO. NON-CPI: N2002-334071

DOC. NO. CPI: C2002-120324

TITLE: Preparing a high-density **functional** slide useful in preparing high-density **bio-chip/microarray**, by coating a sol-gel containing **amine**-group bearing silanes and a solution containing polyaldehyde groups on a substrate.

DERWENT CLASS: A89 B04 D16 P34

INVENTOR(S): CHANG, Y; CHOW, Z; HO, C; JAN, B; KUO, W; LIU, Y; PAN, C; TSAO, J; WU, C

PATENT ASSIGNEE(S): (CHAN-I) CHANG Y; (CHOW-I) CHOW Z; (HOCC-I) HO C; (JANB-I) JAN B; (KUOW-I) KUO W; (LIUY-I) LIU Y; (PANC-I) PAN C; (TSAO-I) TSAO J; (WUCC-I) WU C

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002028506	A1	20020307	(200245)*		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002028506	A1	US 2001-836322	20010418

PRIORITY APPLN. INFO: TW 2000-118070 20000904

AB US2002028506 A UPAB: 20020717

NOVELTY - Preparing (I) a high-density **functional** slide, comprises preparing a sol-gel of silanes in a first solvent, coating the sol-gel onto a substrate (S), removing the first solvent to form an interlayer on the surface of (S), preparing a solution of polyaldehyde groups in a second solvent, coating the solution onto the interlayer to form a polyaldehyde layer, and removing the second solvent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a high-density **functional** slide, comprising (S), an interlayer (IL) of a silane formed by coating a sol-gel of silanes onto (S), and a polyaldehyde layer (PL) formed onto the interlayer;

(2) a **microarray** (II) having high-density **functional** groups for immobilization of a bio-molecule, comprising (S), IL, PL, and a biologically active material, which is immobilized onto PL; and

(3) a polyvinylalcohol (PVA)-based polyaldehyde graft copolymer (III), which is prepared by, dissolving PVA in water to form a polymeric solution, adding the monomer of allyl alcohol and acrolein to the polymeric solution under an anaerobic condition, and adding ceric ammonium nitrate to the solution for catalysis.

USE - (I) is useful for preparing high-density **functional** slide which is useful in the preparation of highly homogenous **functional** group slides and high-density and high-efficiency **bio-chip/microarray**. The high-density **functional** slide facilitates the immobilization of bio-molecules to prepare a **microarray** carrying bio-molecules on it.

ADVANTAGE - (I) rapidly prepares a high-density **functional** slide. The **amine**-group density on the slide can be moderated by adjusting the ratio of each component during sol-gel synthesis. Thus, the subsequent coated polyaldehyde polymer can be properly bonded to and closely linked with the **amine** groups, which increases the distribution of aldehyde density appearing on the slide and strengthening the bonding efficiency between the aldehyde groups and bio-molecules. The time for the production procedure is markedly shortened. As compared with the conventional method in which the bonding is created by a two-step reaction (i.e., by the silane-based polymer and followed by adding a crosslinker), this method reduces the reaction to one-step reaction. The time for the immobilization reaction is only 15 minutes, which is substantial reduction from that of the conventional method, and the efficiency of immobilization is thus markedly increased.

Dwg.0/11

L165 ANSWER 47 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-407210 [44] WPIDS
DOC. NO. CPI: C2002-114489
TITLE: Parallel sequencing of DNA, useful e.g. for detecting point mutations, by nested polymerase chain reaction, using outer primers in solution and immobilized internal

primers.
DERWENT CLASS: A89 B04 D16
INVENTOR(S): SCHNEIDER, S; ZELTZ, P
PATENT ASSIGNEE(S): (BIOC-N) BIOCHIP TECHNOLOGIES GMBH
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1186669	A1	20020313	(200244)*	GE	21
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2002020833	A2	20020314	(200244)	GE	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001087712	A	20020322	(200251)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1186669	A1	EP 2000-119182	20000905
WO 2002020833	A2	WO 2001-EP10160	20010904
AU 2001087712	A	AU 2001-87712	20010904

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001087712	A	Based on	WO 200220833

PRIORITY APPLN. INFO: EP 2000-119182 20000905

AB EP 1186669 A UPAB: 20020711

NOVELTY - Specific determination of DNA sequences (I), comprising parallel amplification in a combined liquid/solid phase **microarray** system, using nested polymerase chain reaction (PCR), with x primer sets (x = number of (I) being determined), each of at least three primers, is new.

DETAILED DESCRIPTION - Specific determination of DNA sequences (I), comprising parallel amplification in a combined liquid/solid phase **microarray** system, using nested polymerase chain reaction (PCR), with x primer sets (x = number of (I) being determined), each of at least three primers, is new. Each primer set comprises:

(a) two outer primers (P1, P2) that hybridize upstream and downstream of the target DNA (A) being amplified; and

(b) an internal primer (P3) that hybridizes to (A) and can form an extension product (EP).

The outer primers are present in the liquid phase, at an excess relative to P3, and P3 are irreversibly bound to a solid phase, forming a **microarray** of x spaced apart and defined positions. Determination is based on detecting an EP from P3 at defined array positions.

INDEPENDENT CLAIMS are also included for the following:

(1) determining point mutations by the novel method;

(2) determining the sequence of (unknown) partial sequences of DNA by the new method; and

(3) solid phase DNA array of P3.

USE - The method is used to determine point mutations, to sequence (unknown) regions of DNA, e.g. in genomics or proteomics analysis, and for diagnostic determination of analytes.

ADVANTAGE - The method is an economical, simple and error-free way for amplifying an array of DNA sequences without compromising sensitivity or specificity. Unlike known nested PCR in the liquid phase, dilution and re-establishment of a reaction mixture after the first reaction are not required, i.e. the total analysis needs only one working operation. The use of high annealing temperatures minimizes non-specific binding, making it possible to measure increases in mass at specific locations by physical methods, e.g. from changes in refractive index.
Dwg.0/5

L165 ANSWER 48 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-332037 [37] WPIDS
DOC. NO. CPI: C2002-095901
TITLE: Preparation of **microarrays** e.g. **biochips**, involves oxidation of chemical groups present upon the support surface and allowing the formation of aldehyde functions at the surface of the solid support.
DERWENT CLASS: B04 D16
INVENTOR(S): HEVESI, L; JEANMART, L; REMACLE, J
PATENT ASSIGNEE(S): (UNOT) ASBL FACULTES UNIV NOTRE DAME DE LA PAIX; (HEVE-I) HEVESI L; (JEAN-I) JEANMART L; (REMA-I) REMACLE J; (UYNO-N) UNIV NOTRE-DAME DE LA PAIX
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1184349	A1	20020306	(200237)*	EN	15
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2002018288	A1	20020307	(200237)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
US 2002076709	A1	20020620	(200244)		
AU 2001050187	A	20020313	(200249)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1184349	A1	EP 2000-870184	20000901
WO 2002018288	A1	WO 2001-BE59	20010406
US 2002076709	A1	US 2001-833030	20010410
AU 2001050187	A	AU 2001-50187	20010406

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001050187	A	Based on	WO 200218288

PRIORITY APPLN. INFO: EP 2000-870184 20000901
AB EP 1184349 A UPAB: 20020613
NOVELTY - Preparation of **microarrays** involves oxidation of chemical groups present on a solid support surface to allow the formation of aldehyde functions upon the surface. The aldehyde functions covalently couples with capture molecules designed for the detection, identification, quantification and/or the recovery of complementary target biological or

chemical molecules.

DETAILED DESCRIPTION - Preparation of **microarrays** involves oxidation of chemical group present on a solid support surface to allow the formation of aldehyde functions upon the surface. The aldehyde functions covalently couples with capture molecules designed for the detection, identification, quantification and/or the recovery of complementary target biological or chemical molecules. The covalent binding results in an array comprising a density of at least 4, 10, 16, 20 or more discrete regions per cm2 of solid support surface. Each of the discrete surface regions are bound with a species of capture molecules.

USE - For preparing **microarrays** e.g. **biochips** or chemochips to detect, quantify and/or recover e.g. **nucleotide** sequences, **ligands** or antibodies (claimed), from sample e.g. detecting transcriptional factors.

ADVANTAGE - The **biochip** or chemochip **microarrays** are improved which has increased detection sensitivity (increased coupling yield and rate of retention) of target molecules upon the **microarrays** of the chips. The method is well suited for construction of large number bound molecules on the surface and its automization, then liberation of chemicals, **peptides**, **ligands**, antigens are easily constructed on such support given the facility of deposit of molecules by robot.

Dwg.0/3

L165 ANSWER 49 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-114573 [15] WPIDS
DOC. NO. CPI: C2002-035286
TITLE: Immobilizing **polypeptides**, by contacting them to anchor molecules having nucleophile, so the ester/thioester groups of the **polypeptides** undergo trans-esterification to attach them to the anchor molecules on the surface.
DERWENT CLASS: B04 D16
INVENTOR(S): NOCK, S; SYDOR, J
PATENT ASSIGNEE(S): (ZYOM-N) ZYOMYX INC
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001098458	A2	20011227	(200215)*	EN	61

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001069906 A 20020102 (200230)
US 2002049152 A1 20020425 (200233)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001098458	A2	WO 2001-US19531	20010619
AU 2001069906	A	AU 2001-69906	20010619
US 2002049152	A1 Provisional	US 2000-212620P	20000619
		US 2001-884269	20010619

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2001069906 A Based on WO 200198458

PRIORITY APPLN. INFO: US 2000-212620P 20000619; US 2001-884269 20010619

AB WO 200198458 A UPAB: 20020306

NOVELTY - Immobilizing a **polypeptide** (I) comprising an ester or thioester (E/T) to a surface, by contacting (I) to an anchor molecule (II) comprising a nucleophilic group (N1) at 2 or 3 position relative to a second nucleophilic group, so the E/T undergoes a trans-esterification reaction with N1 to form an intermediate compound in which (I) is attached to (II) through N1, and attaching (II) to the surface.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an array (A1) of immobilized **polypeptides** attached to a surface (A1 comprises at least a first **polypeptide** species and a second **polypeptide** species and each of the **polypeptide** species are attached to a separate region of the surface in same orientation, and are folded in a secondary structure as required for a biological activity);

(2) an array (A2) of immobilized **polypeptides** attached to a surface which comprises a number of surface regions (each surface region has attached to a **polypeptide** species and a **polynucleotide** that encodes the **polypeptide** species);

(3) screening (M1) a library of **nucleic acids** to identify a **nucleic acids** that encodes a **polypeptide** having a desired activity, by expressing a number of fusion **proteins**, each of which is encoded by an expression cassette that comprises a member of the library of **nucleic acids**, an intein coding region, and an open reading frame that encodes a **polypeptide** that is displayed on a surface of a replicable genetic package (the fusion **proteins** are displayed on the surface of a replicable genetic package) and screening the replicable genetic packages to identify those that display a **polypeptide** having the desired activity;

(4) a **nucleic acid** (III) that comprises an expression cassette, comprising an insertion site at which a **polynucleotide** can be introduced into the expression cassette, an intein coding region (the carboxy terminus of the intein coding region is mutated so that it does not function as a splice junction for intein-mediated cleavage), and an open reading frame that encodes a **polypeptide** that is displayed on a surface of a replicable genetic package (the introduction of a **polynucleotide** at the insertion site results in an open reading frame that encodes a fusion **protein** which comprises a **polypeptide** encoded by the **polynucleotide**) which **polypeptide** is attached at its carboxyl terminus to an amino terminus of the intein, and the surface-displayed **polypeptide** is attached to the carboxy terminus of the intein; and

(5) a kit for use in immobilizing one or more **polypeptides** containing E/T to a surface of a substrate, comprising an anchor molecule reagent for adapting E/T containing **polypeptide** to the surface.

USE - The methods are useful for immobilizing **polypeptides** and for forming arrays of **polypeptides** (claimed). The immobilized **polypeptides** are useful for proteomics and high-throughput screening.

ADVANTAGE - The immobilized **polypeptides** are generally in the same orientation, are of full length and biologically active, and can be readily screened for a desired activity.

DESCRIPTION OF DRAWING(S) - The figure shows the schematic representation of methods for immobilizing a **polypeptide** comprising a thioester or ester to a surface.

Dwg.1/3

L165 ANSWER 50 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-265895 [27] WPIDS
DOC. NO. NON-CPI: N2001-190171
DOC. NO. CPI: C2001-080454
TITLE: Immobilizing affinity **ligand** on thiolated support surface, useful e.g. for producing arrays for hybridization assays, by reaction with acrylamido-derivatized **nucleic acid**.
DERWENT CLASS: A96 B04 D16 S03
INVENTOR(S): ABRAMS, E S; MIELEWCZYK, S; PATTERSON, B C; ZHANG, T
PATENT ASSIGNEE(S): (MOSA-N) MOSAIC TECHNOLOGIES INC; (MOSA-N) MOSAIC TECHNOLOGIES
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001016372	A1	20010308	(200127)*	EN	98

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000069437 A 20010326 (200137)
EP 1208238 A1 20020529 (200243) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001016372	A1	WO 2000-US23627	20000828
AU 2000069437	A	AU 2000-69437	20000828
EP 1208238	A1	EP 2000-957879	20000828
		WO 2000-US23627	20000828

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000069437	A	Based on	WO 200116372
EP 1208238	A1	Based on	WO 200116372

PRIORITY APPLN. INFO: US 2000-177844P 20000125; US 1999-151267P 19990827

AB WO 200116372 A UPAB: 20010518
NOVELTY - Immobilizing an affinity **ligand** (I) by forming a covalent bond between an immobilized thiol group on a solid support and a **nucleic acid** (NA) having an acrylamido functional group.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(a) similar method in which the support carries latent thiol groups and these are activated before reaction with (I) that has at least one alpha , beta -unsaturated carbonyl group;
(b) the preparation a solid support having immobilized thiol groups;
(c) forming an array of **nucleic acid** on a solid support;
(d) the **microarray** produced by method (c);
(e) a kit for immobilizing NA comprising a solid support with immobilized latent thiol groups and instructions for activation;
(f) a kit for attaching NA covalently, comprising a support with immobilized thiol groups and NA derivatized with acrylamido groups; and

(g) detecting and separating target NA using complementary NA immobilized by the new method.

USE - The method is used especially to produce **nucleic acid** (NA) arrays for detection/**separation** of complementary targets, e.g. for detecting contaminants; in medical diagnosis; genetic and physical mapping of genomes; monitoring gene expression and DNA sequencing. Antibodies, carbohydrates and many other compounds may also be used as (I), giving products useful for detection or purification.

ADVANTAGE - The method produces a stable thioether bond; requires only readily available reagents (used as aqueous solutions); provides reproducible (from support to support) immobilization, and substrates with latent thiol groups can be stored for a long time.

Dwg.0/9

L165 ANSWER 51 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-572691 [65] WPIDS
DOC. NO. NON-CPI: N2001-426933
DOC. NO. CPI: C2001-170393
TITLE: New linker system, useful for attaching biomolecules to surfaces, particularly for diagnostic detection or isolation of components of specific binding pairs.
DERWENT CLASS: B04 D16 L03 S03
INVENTOR(S): KLAPPROTH, H
PATENT ASSIGNEE(S): (BIOC-N) BIOCHIP TECHNOLOGIES GMBH
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1132739	A1	20010912	(200165)*	EN	11
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
EP 1132739	B1	20010926	(200165)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2001088535	A1	20011122	(200176)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
DE 60000014	E	20011122	(200201)		
AU 2001074042	A	20011126	(200222)		
ES 2164632	T3	20020301	(200229)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1132739	A1	EP 2000-110428	20000516
EP 1132739	B1	EP 2000-110428	20000516
WO 2001088535	A1	WO 2001-EP5557	20010516
DE 60000014	E	DE 2000-600014	20000516
		EP 2000-110428	20000516
AU 2001074042	A	AU 2001-74042	20010516
ES 2164632	T3	EP 2000-110428	20000516

FILING DETAILS:

PATENT NO	KIND	PATENT NO

DE 60000014 E Based on EP 1132739
AU 2001074042 A Based on WO 200188535
ES 2164632 T3 Based on EP 1132739

PRIORITY APPLN. INFO: EP 2000-110428 20000516
AB EP 1132739 A UPAB: 20011108
NOVELTY - Linker system (I) used to activate surfaces for conjugation with biomolecules (II).

DETAILED DESCRIPTION - Linkers of formula (I) are new X-((Y1)i-Q-(Y2)j)k-Z (I)

X = reactive group that binds covalently to a surface;

Z = reactive group that binds covalently to (II), but is not the same as X;

Y1, Y2 = CR1R2;

R1, R2 = H or 1-4C alkyl, alkoxy or acyloxy;

i, j, k = 1-0, provided that the total number of carbon atoms in Y1, Y2, excluding any in R1 and R2, is 2-100;

Q = hydrophilic atom or group, i.e. O, NH, carbonyl, carbonyloxy or CR3R4; and

R3, R4 = H, OH or 1-4C alkoxy or acyloxy, but not both hydrogen, provisos: when Q = NH, Z is not amino and when k is greater than 1, the Q groups are same or different.

INDEPENDENT CLAIMS are also included for:

(a) surface carrying (I);

(b) a method for detecting or isolating a (II) that is one component of a complementary binding system comprising;

(i) contacting a surface with a sample suspected to contain the complementary binding partner;

(ii) removing non-specifically bound sample components in a washing step; and

(iii) detecting the specifically bound sample components; and

(c) medical or diagnostic instrument that comprises (a).

USE - (I) is used to prepare surfaces for covalent attachment of biomolecules. The surfaces are used for detection and isolation of components of specific binding systems, e.g. as sensor chips or **biochips** for detection and affinity materials for (chromatographic) isolation, particularly of **nucleic acids** or antibodies. The chips are useful in medicine and diagnosis for determining analytes in physiological fluids.

ADVANTAGE - (I) can provide negatively or positively charged, or uncharged, hydrophilic layers, so can be adapted for particular applications. The surface layers are more easily wetted than conventional surfaces, so provide greater density of bound compound and larger dot diameters, thus greater binding to complementary component. This improves precision and/or reduces the space required for serial or parallel determinations. After coating of the surface, no other steps (e.g. coupling to a bifunctional linker) are needed. (I) can be applied by standard printing methods used in preparation of micrometer arrays.
Dwg.0/0

L165 ANSWER 52 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-490942 [43] WPIDS
CROSS REFERENCE: 1999-119865 [10]
DOC. NO. CPI: C2000-147497
TITLE: Reagents and method for covalently attaching target molecules to substrates, useful for the preparation of **nucleic acid microarrays**.
DERWENT CLASS: A89 B04 D16
INVENTOR(S): CHAPPA, R A; GUIRE, P E; HU, S; SWAN, D G; SWANSON, M J
PATENT ASSIGNEE(S): (SURM-N) SURMODICS INC
COUNTRY COUNT: 24
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000040593	A2	20000713	(200043)*	EN	63
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP MX					
AU 2000024979	A	20000724	(200052)		
US 2001014448	A1	20010816	(200149)		
EP 1141385	A2	20011010	(200167)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6465178	B2	20021015	(200271)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000040593	A2		WO 2000-US535	20000110
AU 2000024979	A		AU 2000-24979	20000110
US 2001014448	A1	CIP of	US 1997-940213	19970930
			US 1999-227913	19990108
EP 1141385	A2		EP 2000-903199	20000110
			WO 2000-US535	20000110
US 6465178	B2	CIP of	US 1997-940213	19970930
			US 1999-227913	19990108

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000024979	A	Based on	WO 200040593
US 2001014448	A1	CIP of	US 5858653
EP 1141385	A2	Based on	WO 200040593
US 6465178	B2	CIP of	US 5858653

PRIORITY APPLN. INFO: US 1999-227913 19990108; US 1997-940213 19970930

AB WO 200040593 A UPAB: 20021105

NOVELTY - A reagent (I) and method (II) for attaching target molecules to the surfaces of substrates, are new. (I) comprises functional groups that covalently bond to the target molecule and may optionally comprise photoreactive groups for the same purpose.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a reagent (I) for attaching a target molecule to the surface of a substrate, comprising a polymeric backbone with at least 1 pendent thermochemically reactive group adapted to form covalent bonds with corresponding functional groups on the target molecule and the reagent is adapted to be coated and immobilized onto a surface in a manner that permits:

(a) a small sample volume of a solution containing the target molecule to be applied in the form of a discrete spot on the reagent coated surface;

(b) target molecule present in the sample volume to become attached to the bound reagent by a reaction between its functional groups and the corresponding thermochemically reactive groups; and

(c) substantially all unattached target molecule to be washed from the spot without undue detectable amounts of target molecule in the area surrounding the spot;

(2) a method (II) of attaching a target molecule to the surface of a substrate, comprising:

(a) providing (I) and coating and immobilizing the reagent composition on the substrate surface;

(b) providing a solution comprising a target molecule comprising at least 1 functional group thermochemically reactive with corresponding

groups provided by (I);
(c) applying 1 or more discrete small sample volume spots of the solution to the surface; and
(d) allowing the thermochemically reactive groups provided by (I) to form covalent bonds with corresponding functional groups from the target molecule to attach the target molecule to the surface;
(3) an activated slide (III) with a flat support surface coated with the bound residue of (I); and
(4) a **microarray** (IV) prepared by:
(a) coating and immobilizing (I) on to a substrate surface;
(b) providing a solution comprising a target molecule comprising 1 or more functional groups thermochemically reactive with corresponding groups provided by (I);
(c) applying 1 or more discrete small sample volume spots of the solution to the surface of the substrate; and
(d) allowing the thermochemically reactive groups of (I) to form covalent bonds with corresponding functional groups provided by the target molecule to attach the target molecule to the surface.
USE - The method (II) is used to prepare activated slides for the production of **microarrays** of **nucleic acids** upon the surface of plastic, silicon hydride, silicone and/or organosilane-pretreated glass slides. Each array provides at least 100/cm2 distinct **nucleic acids** with a length of at least 10 **nucleotides**. The **nucleic acids** are each spotted in discrete regions and in defined quantities of 0.1 femtomoles to 10 nanomoles. The regions are circular in shape and have a diameter of 10 to 500 microns and are separated from other regions in the array by a center to center spacing of 20 microns to 100 microns (claimed). The **microarrays** may be used in a range of diagnostic procedures.
(I) may also be used to attach molecules to microwell plates, tubes, beads, silicon wafers and/or membranes.
ADVANTAGE - (I) may be used to attach probes to surfaces which would otherwise absorb them, such as polypropylene and polyvinylchloride. The resultant surfaces provide signals comparable to or better than those obtained with modified **oligonucleotide** absorbed onto polystyrene or polycarbonate. (I) provides improved **nucleic acid** immobilization for solid phase sequencing and for immobilizing primers for polymerase chain reaction (PCR) and other amplification techniques.
Dwg.0/0

L165 ANSWER 53 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-423411 [36] WPIDS
CROSS REFERENCE: 2000-423410 [36]
DOC. NO. NON-CPI: N2000-315917
DOC. NO. CPI: C2000-128230
TITLE: Immobilization of **oligonucleotides** on to a carrier by means of a covalent bond for production of **oligonucleotide microarrays** and chips.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): ASADA, K; KATO, I; KIMIZUKA, F; MINENO, J; OKAMOTO, S; OZAKI, A; UEDA, M
PATENT ASSIGNEE(S): (TAKI) TAKARA SHUZO CO LTD
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000034457	A1	20000615	(200036)*	JA	39

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ

TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000016810 A 20000626 (200045)
EP 1138762 A1 20011004 (200158) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000586891 X 20020326 (200223)
CN 1334872 A 20020206 (200231)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000034457	A1	WO 1999-JP6867	19991208
AU 2000016810	A	AU 2000-16810	19991208
EP 1138762	A1	EP 1999-959692	19991208
		WO 1999-JP6867	19991208
JP 2000586891	X	WO 1999-JP6867	19991208
		JP 2000-586891	19991208
CN 1334872	A	CN 1999-816017	19991208

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000016810	A	Based on	WO 200034457
EP 1138762	A1	Based on	WO 200034457
JP 2000586891	X	Based on	WO 200034457

PRIORITY APPLN. INFO: JP 1998-351276 19981210
AB WO 200034457 A UPAB: 20020516
NOVELTY - Immobilization of **oligonucleotides** on to a carrier comprises mixing the carrier with a buffer containing the **oligonucleotide**, and reacting to fix the **oligonucleotide** to the carrier by means of a covalent bond.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the immobilized **oligonucleotides** produced by the method.
USE - The production of **oligonucleotide** arrays and chips for detection of target **nucleic acids** (such as for the detection of single **nucleotide** polymorphisms).
Dwg.0/0

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